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Synthetic Studies on Wedeligenin: Preparation of 3-Hydroxy-Substituted Decalincarbonitriles as a Model for 'A Ring' Annulation

John K. MacLeod[A,B] *and Tadeusz F. Molinski*[A,C]

[A] Research School of Chemistry, Australian National University, G.P.O. Box 4, Canberra, A.C.T. 2601.
[B] Author to whom correspondence should be addressed.
[C] Present address: Department of Chemistry, University of California, Davis, CA 95616, U.S.A.

Abstract

Six new 3-hydroxydecalincarbonitriles were synthesized by employing an annulation strategy involving intramolecular alkylation of 5-bromoalkyl substituted malononitriles or acetonitriles. 2-Allyl-2-methylcyclohexanone was condensed with malononitrile to give the dialkylcyclohexylidenepropanedinitrile (14). Alternatively, Horner–Emmons–Wittig condensation of the same ketone with diethyl cyanomethylphosphonate gave the corresponding acetonitrile (28). Reduction of the dinitrile with sodium borohydride to give a mixture of *cis* and *trans* cyclohexyl malononitriles followed by epoxidation of the allyl substituent, gave a separable mixture of four epoxides, two of which, (17) and (19), were site-selectively ring-opened to the bromohydrins. Each bromohydrin was quantitatively converted into its respective *O*-trimethylsilyl bromohydrin ether and cyclized to afford the respective decalindicarbonitriles (6) and (7). The substituted acetonitrile (28) was reduced to a 5 : 2 mixture of the corresponding cyclohexylacetonitriles with magnesium in methanol and the products were carried through to their respective *O*-trimethylsilyl bromohydrin ethers and cyclized to afford decalincarbonitriles (8)–(11).

The structure and stereochemistry of the new decalins were assigned by ^{1}H and ^{13}C n.m.r. spectroscopy.

Introduction

The toxic amino glycoside, wedeloside (1) occurs in the leaves and stems of the yellow daisy, *Wedelia asperrima*. Serious sheep losses in north-western Queensland have been caused by ingestion of this plant, and the specific toxicity of *W. asperrima* has been attributed to the presence of wedeloside (1), an amino glycosylated kaurenoid diterpene. The structure of (1) was determined by a combination of n.m.r. and mass spectral analysis combined with chemical degradation.[1] Wedeloside[2] and its well known analogues, atractyloside (2) and carboxyatractyloside (3) are powerful inhibitors of oxidative phosphorylation in mitochondria by virtue of their ability to block ADP/ATP transport by binding to the carrier protein at the outer side of the cell membrane.[3] A structural

[1] Lewis, I. A. S., MacLeod, J. K., and Oelrichs, P. B., *Tetrahedron*, 1981, **37**, 4305; Eichholzer, J. V., Lewis, I. A. S., MacLeod, J. K., and Oelrichs, P. B., *Tetrahedron*, 1981, **37**, 1881.
[2] Klingenberg, M., Appel, M., and Oelrichs, P. B., *FEBS Lett.*, 1985, **189**, 245.
[3] Santi, R., and Luciani, S., (Eds), 'Atractyloside: Chemistry, Biochemistry and Toxicology' (Piccin Editore: Padova 1978) and references cited within.

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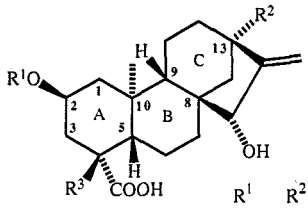
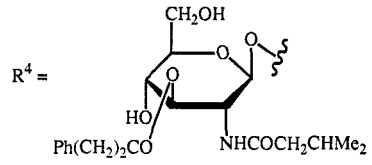
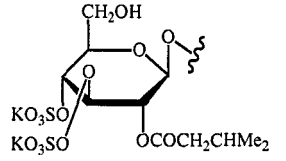
feature crucial to this activity is the presence of the unique tetracyclic *ent* kaurene nucleus bearing a carboxy group at C4 as found in (2) or the 4,4-*gem* dicarboxy group contained in (1) and (3). A total synthesis of atractyligenin, the aglycone of (2), has been reported recently.[4]

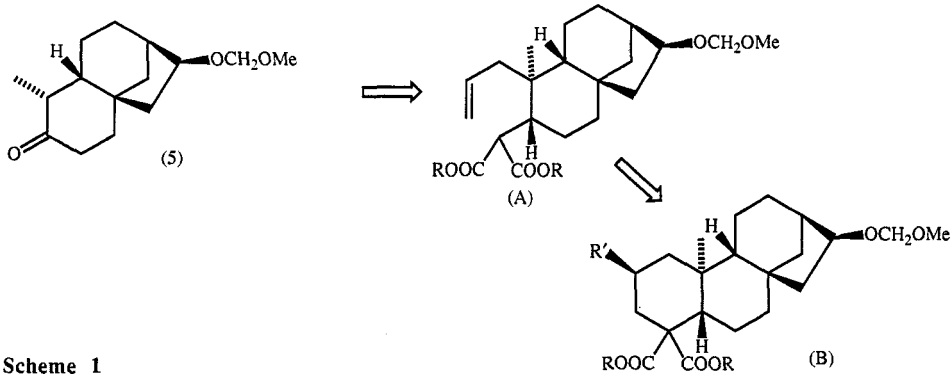


	R^1	R^2	R^3
(1) wedeloside	R^4	OH	COOH
(2) atractyloside	R^5	H	H
(3) carboxyatractyloside	R^5	H	COOH
(4) wedeligenin	H	OH	COOH





In a proposed scheme for the total synthesis of wedeligenin (4), the kaurenoid aglycone of (1), it became important to develop an efficient procedure for the annulation of ring A on a preformed B/C/D tricyclic intermediate which would allow incorporation of the 4,4-dicarboxylic acid and the 2β-hydroxy functional groups. Robinson annulation of the intermediate (5),[5] prepared from 2-naphthol in 13 steps, was only modestly successful, and the need for subsequent 3,2 transposition of the resulting keto group and stepwise introduction of the carboxy groups detracted from this approach. A novel alternative approach, based on introduction of the elements of ring A in three stages (Scheme 1), was proposed: (i) regiospecific alkylation of a suitable tricyclic ketone such as (5) with allyl bromide; (ii) Knoevenagel condensation of a malonate equivalent with the keto group followed by conjugate reduction; and, finally (iii) oxidation of the vinyl group and intramolecular alkylation to complete the six-membered ring. The appeal of this shorter sequence, promising to deliver a product bearing a correctly functionalized A ring, was mitigated by two concerns: (*a*) the stereochemistry of conjugate reduction. The addition of hydrogen to the β face of the conjugated olefin is required in order to achieve the 5β

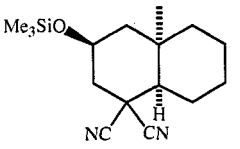


Scheme 1

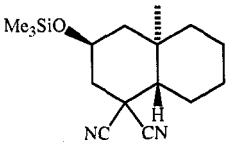
[4] Singh, A. K., Bakshi, R. K., and Corey, E. J., *J. Am. Chem. Soc.*, 1987, **109**, 6187.
[5] Molinski, T. F., Ph.D. Thesis, Australian National University (1984).

configuration present in wedeligenin (4) and other *ent* kaurenoids in general; (*b*) oxidation of the vinyl group and choice of a suitable leaving group at the terminal carbon to ensure facile six-membered ring closure.

In order to test this scheme without sacrificing quantities of intermediate (5), a model study was carried out. The synthesis of simple models of the A/B ring system addressed the above two problems and allowed evaluation of the overall feasibility of the new approach to the synthesis of (4) and its analogues. This paper describes the preparation of a series of 3-hydroxydecalincarbonitriles, (6)–(11), by the successful application of this ring annulation methodology to 2-methylcyclohexanone, and conversion of (6) into the dicarboxylic acid (12).



(6)



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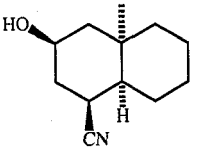

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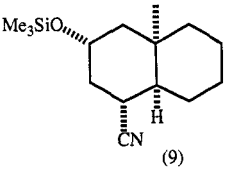

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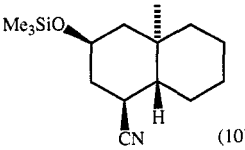

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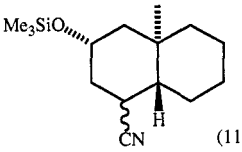

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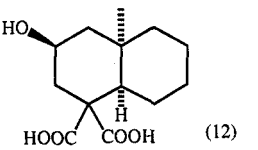


(12)

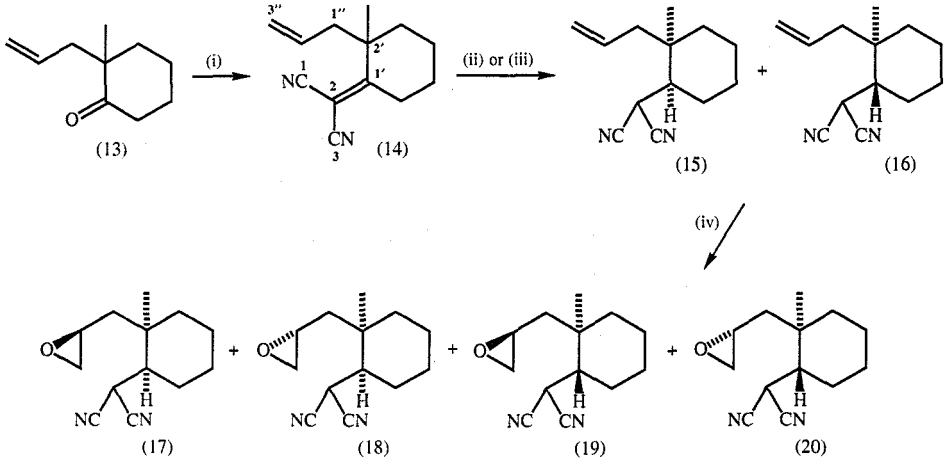
Synthesis of Decalindicarbonitriles (6) and (7)

2-Methylcyclohexanone was chosen as a suitable model for the tricyclic ketone (5). Regioselective alkylation of 2-methylcyclohexanone with allyl bromide afforded 2-allyl-2-methylcyclohexanone (13).[6] Attempted Knoevenagel condensation of ketone (13) with each of diethylmalonate, isopropylidene malonate (Meldrum's acid) or ethyl cyanoacetate failed and returned only starting material. Malononitrile, however, slowly condensed with (13) in the presence of β-alanine/piperidine/acetic acid[7] in boiling benzene to give the dicyanocyclohexylidene (14) in 69% yield (Scheme 2). The ^{13}C n.m.r. spectrum of (14) revealed a highly polarized conjugated carbon–carbon double bond (δ 83·4, s; 188·8, s). This was readily reduced with sodium borohydride in ethanol[8] to give a 9 : 2 mixture of the *cis* (15) and *trans* isomers (16), in 70% combined yield. Separation of (15) from (16) was achieved by repeated medium-pressure liquid chromatography (m.p.l.c.) over silica.

Assignment of the stereochemistry of (15) and (16) followed from inspection of their ^{13}C n.m.r. chemical shifts and multiplicities and subsequent conversion into *cis*- and *trans*-fused decalins, respectively. Assuming both isomers adopt chair conformations in solution, it is expected that the bulkiest substituent, the dicyanomethyl group, is always disposed equatorially. The ^{13}C chemical shift of an axial methyl group on a cyclohexane ring is generally at higher field with respect to that of an equatorial methyl group.[9] It follows that the

[6] Conia, J. M., and Leyendecker, F., *Bull. Soc. Chim. Fr.*, 1967, 830.
[7] Prout, F. S., *J. Org. Chem.*, 1953, **18**, 928.
[8] Camps, P., Ortúno, R. M., and Serratosa, F., *Tetrahedron*, 1976, **32**, 2583.
[9] Wehrli, F. W., and Wirthlin, T., 'Interpretation of Carbon-13 NMR Spectra' p. 43 (Heyden and Son Ltd: London 1974).

trans isomer (16) is identified by the presence of a high-field methyl signal (δ 19·0) and the *cis* isomer (15) is that with the low-field methyl signal (δ 21·0). The remaining ^{13}C n.m.r. signals are fully consistent with these conformations.



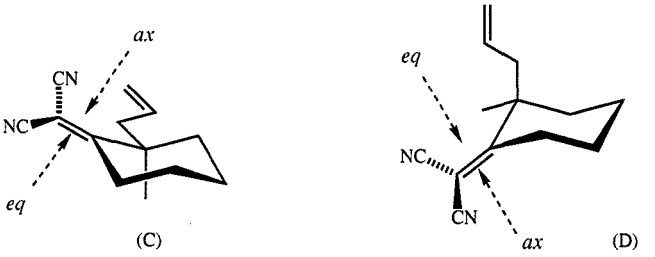
Scheme 2. Reagents: (i) $CH_2(CN)_2$, β-alanine, piperidine acetate, PhH, 80°, 68%; (ii) $NaBH_4$, EtOH, 0°, 70%; (iii) Et_3N, HCOOH, 50°, 90%; (iv) *m*-chloroperoxybenzoic acid, $ClCH_2CH_2Cl$, 4,4′-thiobis(6-t-butyl-3-methylphenol), 75%.

The stereochemical outcome of the borohydride reduction can be shown to be a consequence of a conformational preference of the substituted cyclohexylidene (14). Although little difference may be expected between the steric demand of an allyl group and a methyl group on a *flexible* substituted cyclohexylidene in a pseudo chair conformation, the considerable homoallylic steric strain imposed at the C2 equatorial site by the dicyanomethylidene group forces the less accommodating allyl group into an *axial* orientation. This was supported by molecular mechanics calculations which showed that (14) favours the chair conformation (C) with an axial allyl group over the equatorial axial conformer (D) by 5·1 kJ mol^{-1}. Conjugate reduction of the highly polarized tetrasubstituted carbon–carbon double bond of (14) proceeds by axial attack of borohydride ion,[8,10] analogous to borohydride reduction of simple cyclohexanones, to provide the *cis* isomer as the major product. This outcome is actually favourable because it demonstrates a preference for a product bearing an equatorial propanedinitrile group. It follows that borohydride reduction of a putative tricyclic substrate (e.g. the α,β-unsaturated precursor to (A), Scheme 1) where the conformation of the allyl group would be held rigidly *equatorial*, may be expected to give largely the required *trans* isomer. Alternatively, a higher combined yield (90%) of cyclohexanes (15) and (16) was obtained by reduction of (14) with triethylammonium formate in hot dimethylformamide[11] giving a slightly higher ratio (1 : 3) of *trans* (16) to *cis* (15).

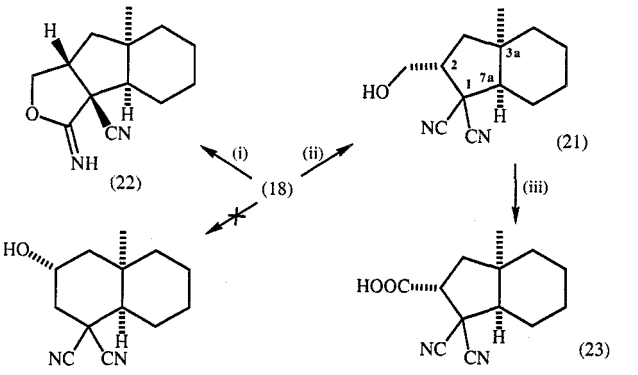
Oxidation of the allyl side chain was conveniently carried out on an unseparated mixture of isomers. Treatment of a mixture of (15) and (16)

[10] Holman, R. J., and Utley, J. H. P., *Tetrahedron Lett.*, 1974, 1553.
[11] Nanjo, K., Suzuki, K., and Sekiya, M., *Chem. Pharm. Bull.*, 1977, **25**, 2396.

with *m*-chloroperoxybenzoic acid in boiling 1,2-dichloroethane containing a trace of radical inhibitor[12] afforded a mixture of four diastereomeric epoxides, (17)–(20), in good yield (70% combined). These were separated by repetitive m.p.l.c. over silica. The major diastereoisomers were (17) and its epimer (18), formed in equimolar amounts, and these were shown to be derived from the *cis* cyclohexanedinitrile (15). Epoxidation of pure (15) under the same conditions gave only (17) and (18) in an equimolar ratio, showing no diastereoselection at C 2′.



The stage was set for annulation but the closure of the second ring proved somewhat capricious. Although epoxide (19) possesses the correct relative stereochemistry, corresponding to that required for wedeligenin (4), subsequent trial reactions were also carried out on the more abundant isomers (17) and (18). Mild base treatment (KBr, *dry* dimethylformamide) of (18) gave a high yield of the dinitrile (21) (Scheme 3). Other basic conditions (e.g. K_2CO_3, MeOH; KNH_2, NH_3(liquid); NaH, tetrahydrofuran; Et_3N, benzene; LiBr, tetrahydrofuran; lithium *N*-isopropyl-*N*-cyclohexylamide, tetrahydrofuran) gave only the imino lactone (22) arising from initial formation of (21) followed by intramolecular addition of the hydroxymethylene group to one of the nitriles. Imino lactones were also formed spontaneously from (18)–(20) upon prolonged standing (*c.* 3 months) at 4°.



Scheme 3. Reagents: (i) K_2CO_3/MeOH or KNH_2/NH_3 or NaH/tetrahydrofuran or $NaOCMe_2C_2H_5$/PhH or Et_3N/PhH or $KOBu^t$/dimethylformamide or lithium *N*-isopropyl-*N*-cyclohexylamide/–78°/tetrahydrofuran; (ii) KF/dimethylformamide/23° or Bu_4NBr/dimethylformamide/60°; (iii) Jones oxidation.

[12] Kishi, Y., Aratani, M., Tanino, H., Fukuyama, T., Goto, T., Inoe, S., Sugiura, S., and Kakoi, H., *Chem. Commun.*, 1972, 64.

The products of treatment of (17) or (18) with base were dependent upon reaction conditions. Each however arose from *exo* attack of the incipient carbanion upon the tertiary carbon of the epoxide, giving an unwanted substituted hydrindane. This is predicted from Baldwin's general rules[13] for ring closure and has been rationalized on stereoelectronic grounds[14] although exceptions are known.[15] The structure of (21) was established by examination of the ^{1}H n.m.r. spectrum and Jones oxidation to the carboxylic acid (23) (Scheme 3). Tentative assignment of *cis-anti-cis* stereochemistry in (22) is based on presumed inversion at the tertiary epoxide carbon followed by backside attack of the liberated alkoxide anion on the proximal nitrile, however, this remains to be proved.

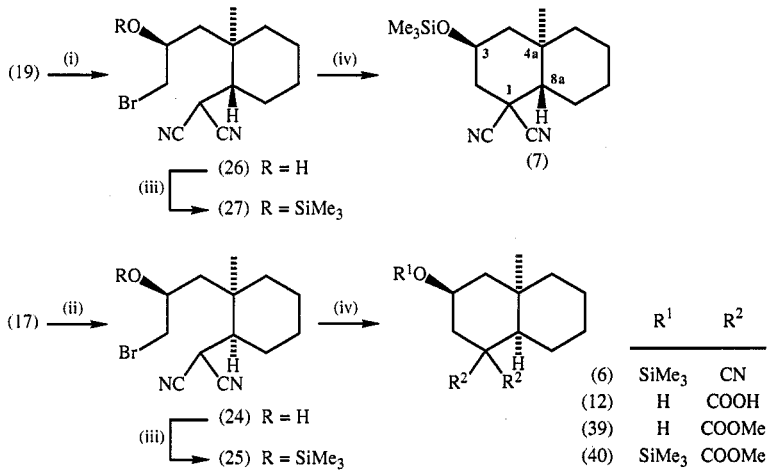
The problem of unwanted formation of a five-membered ring from (17) or (18) due to the ambident nature of the electrophilic epoxide was effectively solved by changing the epoxide to a bromohydrin, a more compliant functionality, bearing a leaving group at the terminus of the side chain. Brief exposure of (17) to hydrogen bromide gave the bromohydrin (24) in 71% yield (Scheme 4). Alternatively, this conversion could be achieved in good yield under mild conditions by treatment of epoxide (17) with lithium tetrabromonickelate(II), a reagent developed in this study for the regioselective opening of epoxides.[16] The bromohydrin (24) was protected (trimethylsilylimidazole, tetrahydrofuran) by conversion into the *O*-trimethylsilyl derivative (25) in quantitative yield. Failure to protect the hydroxy group of (24) prior to ring closure with base (K_2CO_3/MeOH) resulted in the formation of (22). Evidently, carbocyclic ring closure is not competitive with elimination of HBr from the bromohydrin (24) which, under these basic conditions, returns to the epoxide (17). Rapid base-catalysed isomerization of (17) then follows as described above, first forming (21) and, ultimately, (22). Trimethylsilyloxy dinitrile (25) was smoothly and quantitatively converted into the 3β-hydroxy-*cis*-decalin (6) with potassium carbonate in dry dichloromethane under reflux. The same sequence was applied to the minor epoxide (19) to give the corresponding 3β-hydroxy-*trans*-decalindicarbonitrile (7) (Scheme 4).

Synthesis of Decalincarbonitriles (8)–(11)

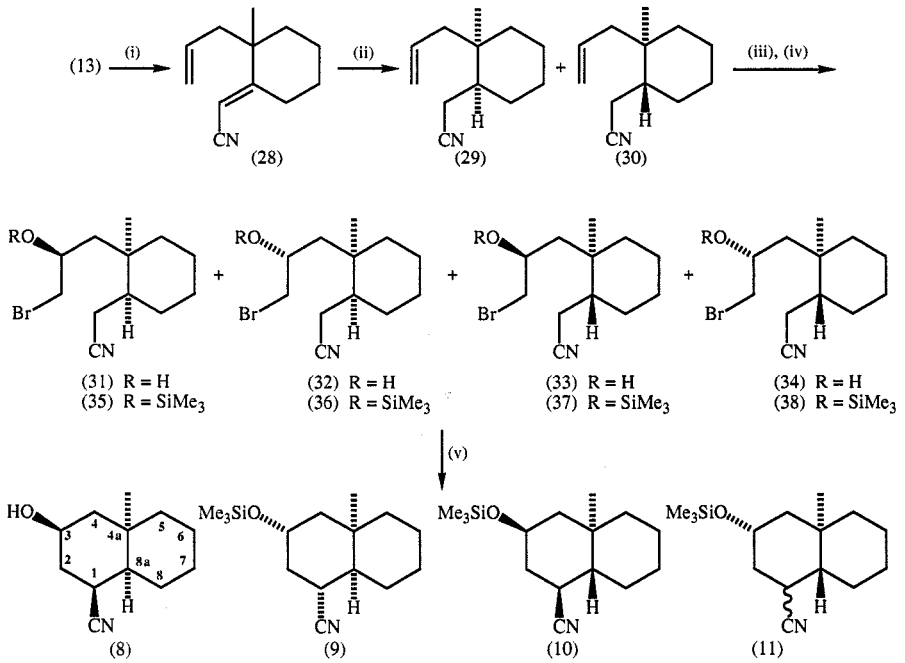
The slow rate of Knoevenagel condensation of (13) with malononitrile, assumed to be a result of steric hindrance at the carbonyl group, would present an obstacle to the application of the above described ring A annulation for the synthesis of wedeligenin (4). Indeed, when (5) was subjected to similar condensation conditions only starting material was obtained,[5] even after 48 h. To circumvent this problem it was decided to try to introduce only one nitrile prior to completion of ring A. Introduction of the second carboxylate equivalent would be postponed to a later stage.

The syntheses of decalincarbonitriles (8)–(11) were carried out in a similar manner to that of (6) and (7) with some minor modifications (Scheme 5). Ketone (13) readily condensed with the ylid generated ($NaNH_2$, tetrahydrofuran) from diethyl cyanomethylphosphonate[17] to give a single compound, the conjugated

[13] Baldwin, J. E., *Chem. Commun.*, 1976, 734.
[14] Stork, G., Cama, L. D., and Coulson, D. R., *J. Am. Chem. Soc.*, 1974, **96**, 5270, 5628.
[15] See, for example Lallemand, J. Y., and Onanga, M., *Tetrahedron Lett.*, 1975, 585.
[16] Dawe, R. D., Molinski, T. F., and Turner, J. V., *Tetrahedron Lett.*, 1984, **25**, 2061.
[17] Bose, A. K., and Dahill, R. T. Jr, *J. Org. Chem.*, 1965, **30**, 505.



Scheme 4. Reagents: (i) $Li_2[NiBr_4]$, tetrahydrofuran, room temperature, 60%; (ii) HBr, AcOH, CH_2Cl_2, −30°, 70%; (iii) *N*-trimethylsilylimidazole, tetrahydrofuran, 30 min, quantitative; (iv) K_2CO_3, 18-crown-6, CH_2Cl_2, reflux, quantitative.



Scheme 5. Reagents: (i) $(EtO)_2POCH_2CN$, $NaNH_2$, tetrahydrofuran, 93%; (ii) Mg, MeOH, 89%; (iii) *N*-bromosuccinimide, dioxan, H_2O, 55%; (iv) *N*-trimethylsilylimidazole, tetrahydrofuran, quantitative; (v) $LiN(SiMe_3)_2$, tetrahydrofuran/n-hexane, 60–100%.

nitrile (28) (93%), presumably the *E* isomer. The conjugated double bond of (28), being less polarized, was reduced this time with magnesium in methanol[18] to afford a mixture (5 : 2 *cis* to *trans*, 89% combined yield) of carbonitriles (29) and (30). Direct oxidation of this mixture with *N*-bromosuccinimide gave a mixture of four bromohydrins (31)–(34) (55% combined yield) which were carefully separated by m.p.l.c. over silica. Bromohydrins (31) and (34) were obtained as a 5 : 1 mixture and were used without further separation in the subsequent steps. After protection as their respective *O*-trimethylsilyl ethers (35)–(38), the nitriles were cyclized (lithium hexamethyldisilazide, tetrahydrofuran, −30°) to give their respective decalincarbonitriles (8), (9), (10) and (11) in good yield (63–100%). It is interesting to note that in the case of compound (35) cyclization was accompanied by loss of the trimethylsilyl group, giving the hydroxy compound (8).

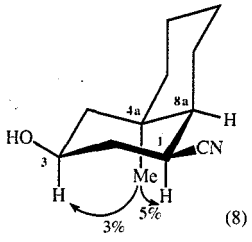
Assignment of Stereochemistry of Decalins (6)–(11)

The complete relative configurations of decalins (6)–(11) were obtained after careful analysis and assignment of their ^{1}H n.m.r. and ^{13}C n.m.r. spectra together with selected nuclear Overhauser effect difference spectroscopy (n.O.e.d.s.) experiments.[19] Firstly, ^{13}C n.m.r. was used to assign the ring junction stereochemistry of the decalins. Dalling and Grant[20] showed that in simple 9-methyldecalins the ^{13}C chemical shift of the angular methyl group is highly dependent upon the stereochemistry of the ring junction, occurring consistently at higher field in the *trans* series because of the increased number of 1,3-diaxial steric interactions. Decalindinitrile (6) exhibits a quaternary methyl signal at δ 29·3 and is assigned a *cis* ring junction while decalin (7) shows this signal at δ 18·0 and this isomer, therefore, is *trans*. The C3 configuration of decalin (7) was assigned from examination of the ^{1}H n.m.r. spectrum. The H3 signal (δ 4·07, tt, J 11·5, 4·4 Hz) of (7) displays a typical coupling pattern for an equatorial C3 substituent flanked by two methylene groups, namely two large axial–axial vicinal couplings and two smaller axial–equatorial couplings. This is commonly seen in the ^{1}H n.m.r. spectra of 3β-hydroxy steroids[21] and 2β-hydroxy kaurenoids,[1] hence, decalin (7) has the 3β-hydroxy configuration. The case for decalin (6) is less clear. Unlike the rigid *trans* decalin ring system, the flexible *cis* stereochemistry allows for inversion of ring conformation so that both 3β and 3α substituents can adopt the preferred equatorial disposition. Nevertheless, the 3β configuration could confidently be assigned to the trimethylsilyloxy substituent of (6) based upon comparison of the ^{13}C n.m.r. spectrum of this compound with that of the 3β-hydroxydecalincarbonitrile (8), the stereochemistry of which was determined as described below.

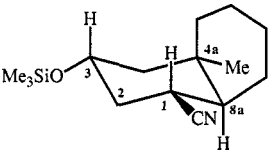
The stereochemistry of the nitriles (8)–(11) was assigned by n.m.r. by using arguments analogous to those applied to (6) and (7). However, additional information was now available from their ^{1}H n.m.r. spectra which allowed unambiguous assignment of complete relative stereochemistry and, by analogy,

[18] Profitt, J. A., and Watt, D. S., *J. Org. Chem.*, 1975, **40**, 127.
[19] Hall, L. D., and Saunders, J. K. M., *J. Am. Chem. Soc.*, 1980, **102**, 5703.
[20] Dalling, D. K., Grant, D. M., and Paul, E. G., *J. Am. Chem. Soc.*, 1973, **95**, 3718.
[21] Bhacca, N. S., and Williams, D. H., 'Applications of NMR Spectroscopy in Organic Chemistry' pp. 80–81, 179–180 (Holden-Day: San Francisco 1964).

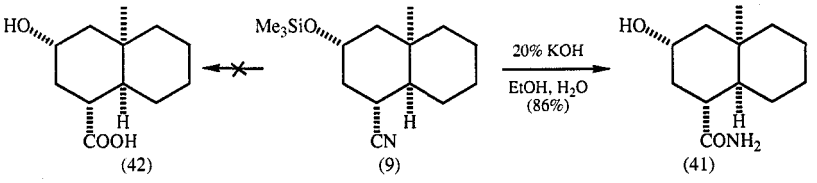
the C3 configuration of dinitrile (6). It was assumed at the outset that the fused cyclohexane rings of decalins (8)–(11) adopted the stable chair conformation and this was supported by the observation of proton coupling constants fully consistent with this hypothesis. The H1 methine proton (δ 2·3–3·1) appeared in each of nitriles (8)–(10) as a multiplet with at least one axial–axial coupling, indicating an equatorial disposition of the cyano group, while the H1 signal for nitrile (11) suggested a mixture of axial and equatorial epimers at C1. The signal for H3 in each of the *cis* decalins (8) and (9) appeared as a one proton triplet of triplets ($J \approx 11$, 5 Hz) at approximately δ 4·0, indicative of equatorial C3 substituents in each but with different chair–chair conformations. H1 in (8) (δ 3·07, dt, J 13·5, 5·0 Hz) displayed coupling to an equatorial bridgehead (H8a) proton and therefore it follows that (8) is the 3β-hydroxy isomer with a *cis* fused ring. This was verified by n.O.e.d.s. experiments. Irradiation of the axial C4a methyl in (8) gave 3 and 5% enhancements of the axial proton signals, H3α and H1α, respectively. Similar analysis of vicinal coupling constants of the other *cis* fused epimer (9) also showed an equatorial C3 substituent, verifying the alternative *cis* decalin conformation and, therefore, the 3α-trimethylsilyloxy compound. As expected, irradiation of the C4a methyl group in (9) produced no n.O.e. enhancements of H1β nor of H3β. Detailed ^{13}C n.m.r. analysis of (8) and (9) was entirely consistent with these assignments and, furthermore, comparison of the ^{13}C n.m.r. spectrum of (8) with that of (6) showed both compounds possessed the C3β configuration. The stereochemistry of the minor *trans* decalins (10) and (11) was also determined in a similar manner.



(8)



(9)



(42) (9) (41)

Scheme 6

Completion of the model synthesis required conversion of the nitrile groups into carboxylic acids. Hydrolysis of dinitrile (6) (2% KOH, H_2O, EtOH, reflux, 21 h) gave dicarboxylic acid (12) along with several partially hydrolysed intermediates. This mixture was most easily analysed by g.l.c./m.s. after methylation (CH_2N_2) to the dimethyl ester (39) and silylation (bistrimethylsilyltrifluoroacetamide, pyridine). The predominant component was the expected trimethylsilyl derivative (40) (*m/z* 340, *c.* 1%, M) of the bis(methyl ester) (51%) (Scheme 4).

Nitrile (9) was more resistant to hydrolysis. Treatment of (9) with alkali (20% KOH, aqueous ethanol, 6 h) gave largely the corresponding primary amide (41) (86%) (Scheme 6). Presumably, hydrolysis of (9) under more forcing conditions (e.g. KOH, 1,2-dihydroxypropane, H_2O) would be required for the conversion of (41) into the required monocarboxylic acid (42).

Conclusion

Successful synthesis of decalincarbonitriles (8)–(11) and dinitriles (6) and (7) augured well for the ring A construction proposed in the synthesis of (4). The demonstrated conjugate reduction methodology can be expected to provide the correct stereochemistry at C5 (kaurene ring numbering) and the remainder of the annulation is shown to proceed smoothly. A drawback is the non-stereoselective oxidation of the allyl group, which will necessitate separation of the unwanted isomer and inversion at C2. Use of a more sterically discriminating oxidant (e.g. OsO_4) on the allyl keto intermediate (5) may provide a more favourable C2 isomer ratio.[22]

Experimental

Melting points are uncorrected. Infrared spectra were measured with a Perkin Elmer 257 infrared spectrophotometer. Ultraviolet spectra were measured with a Varian DMS-90 spectrophotometer. ^{1}H n.m.r. spectra were measured in $CDCl_3$ solution unless otherwise stated by using the following instruments at their respective proton fields; 60 MHz with a JEOL JNM-PMX60, or at 100 MHz with a JEOL 'minimar' MH-100 or at 200 MHz with a JEOL PNM FX-200, the majority being run on the last. Broad band decoupled ^{13}C n.m.r. spectra were measured at 50·3 MHz with the JEOL FX 200 instrument and multiplicities were assigned from refocussed INEPT[23] spectra. Analytical g.l.c. was performed by employing a glass packed column (2 m by 2 mm) packed with Chromosorb W, coated with 2% OV-17, employing helium as carrier gas, and carried out by using one of the following instruments; Varian Vista 6000, Varian 1400 or a Perkin Elmer 900. G.l.c./m.s. was carried out by using the above packed column and a Varian MAT III instrument. Mass spectra were recorded on a VG-Micromass 7070F double focussing instrument linked to an Incos data system. Electron impact mass spectrometry (e.i.m.s.) was carried out at 70 eV and chemical ionization mass spectra (c.i.m.s.) were measured with ammonia as reagent gas. Thin-layer chromatography (t.l.c.) was performed on silica gel (Whatman precoated slides, 75 by 25 mm). Preparative-layer chromatography (p.l.c.) was performed on Merck precoated plates (20 by 20 by 0·2 cm of Kieselgel 60 F254 or aluminium oxide 60 F254). Chromatograms were visualized under ultraviolet light or upon exposure to iodine vapour or after first spraying with 5% vanillin in sulfuric acid or 5% phosphomolybdic acid in ethanol then heating. Tetrahydrofuran was distilled from sodium benzophenone ketyl and other solvents were purified and dried by using standard procedures.[24] Microanalyses were carried out by the Australian National University Analytical Service Unit. Force field minimization calculations were carried out on a Silicon Graphics Iris 3130 work station by using CHARMm, Version 2.1 (Newton–Raphson algorithm) and standard parameters for bond lengths, torsion angles and constrained planarity of the conjugated π system [observed for (14) λ_{max} 244 nm, ϵ 12600].

[2′-Methyl-2′-(prop-2″-enyl)cyclohexylidene]propanedinitrile (14)

Procedure 1.—A mixture of 2-(prop-2′-enyl)-2-methylcyclohexanone (13) (10·0 g, 0·066 mol), distilled propanedinitrile (4·36 g, 0·066 mol), β-alanine (2·5 g, 0·028 mol) and acetic acid (6·5 ml) in benzene (100 ml) was heated at reflux with azeotropic removal of water[7] for 24 h. Piperidine (2 ml) was added and heating continued for a total of 48 h at which time

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1 ml of water had collected. The mixture was cooled and washed sequentially with water, saturated sodium bicarbonate solution and water, and dried ($MgSO_4$). The solvent was removed under vacuum to give a dark brown oil (13·2 g) which was fractionally distilled to afford *[2′-methyl-2′-(prop-2″-enyl)cyclohexylidene]propanedinitrile* (14) as a light yellow oil (9·1 g, 69%). This solidified upon cooling to −15° and was recrystallized twice from n-pentane affording colourless prisms, m.p. 18·5–19° (Found: C, 78·0; H, 8·0; N, 13·7. $C_{13}H_{16}N_2$ requires C, 78·0; H, 8·1; N, 14·0%). ν_{max} (neat) 3080, 2230, 1680, 1575 cm^{-1}. λ_{max} 244 nm (ϵ 12600). ^1H n.m.r. δ 1·49, s, 3H, Me; 1·6–3·0, m, 10H; 5·19, m, 2H; 5·69, m, 1H. ^{13}C n.m.r. δ 20·0, t; 25·9, t; 25·9, q; 33·3, t; 39·5, t; 43·4, t; 44·2, s; 83·4, s, C2; 113·2, s, C1,3; 119·6 t, C3″; 131·8 d, C2″; 188·8, s, C1′. E.i.m.s. *m/z* 200 (M, 62%), 159 (M−C_3H_5, 100).

Procedure 2.—A mixture of ketone (13) (56·7 mg, 0·37 mmol), propanedinitrile (29·5 mg, 0·45 mmol), β-alanine (5 mg), acetic acid (0·05 ml), dried, powdered molecular sieves (4 Å, 70 mg), and ethanol (3·0 ml) were heated at reflux for 60 h under nitrogen. The mixture was cooled, filtered (Celite) and the residue washed with ether. The combined filtrate and washings were concentrated and separated by preparative t.l.c. (silica, dichloromethane) to afford the dinitrile (14) as a yellow oil (33 mg, 44%), identical with an authentic sample by t.l.c. and ^1H n.m.r.

Sodium Borohydride Reduction of Dinitrile (14)

Dinitrile (14) (1·50 g, 7·5 mmol) was dissolved in dry ethanol (50 ml) and the solution cooled to 0°. Sodium borohydride (0·28 g, 7·5 mmol) was added in portions over 30 min with stirring.[8] After an additional 15 min, cold saturated ammonium chloride solution was added and the mixture concentrated under vacuum and extracted three times with ether. The combined ether extracts were washed with water, dried ($MgSO_4$) and evaporated to give a pale yellow oil (1·42 g) which was purified by flash chromatography (silica, toluene) to obtain *dinitriles* (15) and (16) as a 9 : 2 mixture. A sample was repeatedly subjected to m.p.l.c. (silica, 1 : 2 : 7 dichloromethane, ether, n-hexane) to give, in order of elution: (i) trans-*(2′-Methyl-2′-(prop-2″-enyl)cyclohexyl)propanedinitrile* (16). A colourless oil (112 mg) which migrated as a single spot on t.l.c. with the above solvent (R_F 0·8) (Found: C, 77·3; H, 9·2. $C_{13}H_{18}N_2$ requires C, 77·2; H, 9·0%). ν_{max} (neat) 3080, 2255, 1640 cm^{-1}. δ (C_6D_6) 0·66, s, 3H, Me; 0·6–1·7, m, 11H; 3·15, d, 1H, *J* 1·7 Hz, CH(CN)$_2$; 4·9, m, 2H, $W_{h/2}$ 45 Hz, (H3″)$_2$; 5·42, m, 1H, H2″. δ_C (C_6D_6) 19·0, q, Me; 21·3, t, C4; 23·7, d, C2; 25·4, t, C5′; 25·6, t, C6′; 36·7, s, C2′; 37·9, t, C3′; 45·8, d, C1; 46·3, t, C1″; 112·9, s, CN; 114·2, s, CN; 118·7, t, C3″; 133·2, d, C2″. E.i.m.s. *m/z* 187 (M−Me, 1·2%), 161 (M−C_3H_5, 41), 95 (100); (ii) cis-*(2′-Methyl-2′-(prop-2″-enyl)cyclohexyl)propanedinitrile* (15). A colourless oil (272 mg) which migrated as a single spot on t.l.c. (R_F 0·73) (Found: C, 77·3; H, 9·2. $C_{13}H_{18}N_2$ requires C, 77·2; H, 9·0%). ν_{max} (neat) 3080, 2255, 1640 cm^{-1}. δ (C_6D_6) 0·59, s, 3H, Me; 0·7–1·7, m, 10H; 2·21, dd, 1H, *J* 13·5, 7·8 Hz, H1″; 3·34, d, 1H, *J* 2 Hz, CH(CN)$_2$; 4·96, m, 2H, $W_{h/2}$ 28 Hz, (H3″)$_2$; 5·38, m, 1H, H2″. E.i.m.s. *m/z* 187 (M−Me; 0·7%), 161 (M−C_3H_5, 37), 95 (100). C.i.m.s. (NH_3) of a mixture of (8) and (9) gave *m/z* 220 (M+NH_4), 203 (MH).

Reduction of Dinitrile (14) with Triethylamine/Formic Acid Azeotrope

Triethylamine/formic acid azeotrope (b.p. 104°/20 mm Hg, 430 mg, 5 mmol HCOOH) was added to a stirred solution of (14) (181 mg, 0·91 mmol) in dimethylformamide (5 ml).[11] The mixture was heated (50–60°) for 1·5 h then poured into ice-water (40 ml). The mixture was extracted with n-pentane and the combined organic extracts were washed with water (twice), dried ($MgSO_4$) and evaporated to give a colourless oil (175 mg, 96%), comprising an 11 : 4 mixture of (15) and (16) (t.l.c., i.r., ^1H n.m.r.).

Epoxidation of Olefins (15) and (16)

A mixture (9 : 2) of (15) and (16) (2·58 g, 12·8 mmol), *m*-chloroperoxybenzoic acid (85%, 2·85 g, 14·1 mmol) and 4,4′-thiobis(6-t-butyl-3-methylphenol) (29 mg, 1% w/w) in 1,2-dichloroethane was heated at reflux under nitrogen for 2 h.[12] The solution was cooled,

poured onto ice-water then the mixture extracted twice with dichloromethane. The combined organic layers were washed with 0·5 M sodium sulfite solution, 5% sodium chloride solution, dried ($MgSO_4$) and the solvent was removed under vacuum to afford a crude mixture of the four diastereomeric epoxides (17)–(20) as a viscous yellow oil (2·80 g). A portion of the oil (2·63 g) was separated by repeated m.p.l.c. (silica, 1 : 96 ethyl acetate/dichloromethane) to give the following in order of elution. (i) A yellow solid (0·164 g) which was shown by n.m.r. to contain a mixture of compounds but no epoxides. This was not further characterized. (ii) A pale yellow solid (0·266 g). Crystallization from dichloromethane/n-hexane provided pure *(1′R*,2′R*,2″S*)-[2′-(2″,3″-epoxypropyl)-2′-methylcyclohexyl]propanedinitrile* (19) as colourless prisms, m.p. 108° (dec.) (Found: C, 71·2; H, 8·6; N, 13·0. $C_{13}H_{18}N_2O$ requires C, 71·5; H, 8·3; N, 12·8%). ν_{max} ($CHCl_3$) 3050, 2260 cm^{-1}. ^1H n.m.r. δ 1·08, s, Me; 1·2–2·1, m, 10H; 2·27, ddd, J 12·4, 3·4, 2·0 Hz, H1″; 2·47, dd, J 5·1, 2·6 Hz, 1H, H3″$_a$; 2·83, dd, J 5·1, 4·0 Hz, 1H, H3″$_b$; 3·05, m, H2″; 4·14, d, J 2·0 Hz, $CH(CN)_2$. ^{13}C n.m.r. δ 20·41, q, Me; 21·37, t, C4′; 24·21, d, **C**H(CN)$_2$; 24·88, t, C5′ or C6′; 25·84, t, C6′ or C5′; 37·26, s, C2′; 38·48, t, C3′; 45·20, t, C1′; 45·58, d, C2″; 46·16, t, C3″; 47·86, d, C1′; 112·65, s, CN; 114·00, s, CN. E.i.m.s. *m/z* 218 (M, 0·8%), 203 (M−Me, 6), 160 (26), 109 (40), 95 (100). (iii) *(1′R*,2′S*,2″S*)-[2′-(2″,3″-epoxypropyl)-2′-methylcyclohexyl]propanedinitrile* (18), low melting solid (0·685 g) (Found: M$^{+\bullet}$, 218·1419. $C_{13}H_{18}N_2O$ requires 218·1419). ν_{max} (neat) 3050, 2260 cm^{-1}. ^1H n.m.r. δ 1·18, s, Me; 1·2–2·1, m, 11H; 2·47, dd, J 4·8, 2·6 Hz, 1H, H3″$_a$; 2·77. dd, J 4·8, 4·3 Hz, 1H, H3″$_b$; 2·92, m, H2″; 3·89, d, J 2·2 Hz, $CH(CN)_2$. ^{13}C n.m.r. δ 21·29, t, C4′; 23·83, d, **C**H(CN)$_2$; 25·08, t, C5′ or C6′; 25·70, t, C6′ or C5′; 27·53, q, Me; 34·43, t, C1″; 36·91, s, C2′; 37·81, t, C3′; 46·19, t, C3″; 48·47, d, C2″; 50·34, d, C1′; 112·4, s, CN; 113·96, s, CN. E.i.m.s. *m/z* (M, <0·2%), 189 (40), 160 (6), 109 (13), 95 (100). (iv) A colourless low melting solid (1·00 g) containing *(1′R*,2′S*,2″R*)-[2′-(2″,3″-epoxypropyl)-2′-methylcyclohexyl]propanedinitrile* (17) and about 20% of *epoxide* (20). Repeated chromatography (silica, 1 : 1 : 4 dichloromethane/ether/n-hexane) provided pure (17) (Found: M$^{+\bullet}$, 218·1420. $C_{13}H_{18}N_2O$ requires 218·1419). ν_{max} ($CHCl_3$) 3050, 2255 cm^{-1}. ^1H n.m.r. δ 1·21, Me; 1·1–1·2, m, 10H; 2·09, dd, J 14·6, 3·2 Hz, H1″; 2·49, dd, J 4·9, 2·7 Hz, 1H, H3″$_a$; 2·79, dd, J 4·9, 4·2 Hz, 1H, H3″$_b$; 2·95, m, H2″; 4·05, d, J 2·4 Hz, $CH(CN)_2$. ^{13}C n.m.r. δ 21·99, t, C4′; 23·77, d, **C**H(CN)$_2$; 25·32, t, C5′ or C6′; 25·17, t, C6′ or C5′; 27·65, q, Me; 35·04, t, C1″; 36·94, s, C2′; 37·49, t, C3′; 46·83, t, C3″; 48·41, d, C2″; 49·81, d, C1′; 111·42, s, CN; 111·38, s, CN. E.i.m.s. *m/z* 218 (M, 3%), 203 (M−Me, 13), 189 (38), 160 (30), 95 (100). (v) *(1′R*,2′R*,2″R*)-[2′-(2″,3″-epoxypropyl)-2′-methylcyclohexyl]propanedinitrile* (20), low melting solid. (Found: M$^{+\bullet}$, 218·1420. $C_{13}H_{18}N_2O$ requires 218·1419). ν_{max} ($CHCl_3$) 3050, 2255 cm^{-1}. ^1H n.m.r. δ 1·16, s, Me; 1·0–2·1, m, 11H, 2·50, dd, J 4·5, 2·6 Hz, 1H, H3″$_a$; 2·85, dd, J 4·7, 4·3, 1H, H3″$_b$; 3·01, m, H2″; 4·24, d, J 1·7 Hz, $CH(CN)_2$. E.i.m.s. *m/z* 218 (M, 3%), 217 (2), 203 (10), 122 (36), 109 (52), 95 (100). Combined yield was 1·95 g (75%, based upon separated epoxides).

(2α,3aα,7aα)-2-(Hydroxymethyl)-3a-methyl-octahydro-1H-indene-1,1-dicarbonitrile (21)†

A solution of epoxide (18) (28·4 mg, 0·13 mmol) in dry dimethylformamide (1·0 ml) was added to a stirred suspension of dried potassium fluoride (13 mg, 0·22 mmol) in dry dimethylformamide (0·5 ml) at 20° under nitrogen. After 3 h, water (10 ml) was added and the mixture extracted with ether (3×5 ml). The combined ether layers were washed three times with water, dried (Na_2SO_4) and evaporated to give a colourless oil. This was subjected to m.p.l.c. (3 : 13 ethyl acetate/dichloromethane) to give the *hydrindane* (21) (14·5 mg, 51%). Hydrindane (21) was crystallized from dichloromethane/n-hexane as colourless rosettes, m.p. 99–102° (Found: M$^{+\bullet}$, 218·1416. $C_{13}H_{18}N_2O$ requires 218·1419). ν_{max} ($CHCl_3$) 3620, 2250 cm^{-1}. ^1H n.m.r. δ 1·21, s, Me; 1·2–2·0, m, 10H; 1·57, br s, 1H, OH; 2·23, dd, J 6·5, 6·5 Hz, H7aα; 2·91, m, H2β; 3·92, m, C**H**$_2$OH. Irradiation of the signal at δ 3·92 caused collapse of the signal at 2·91 to a dd, J 12, 8 Hz. Irradiation of the signal at δ 2·91 caused collapse of the signal at 3·92 to a broad singlet. ^{13}C n.m.r. δ 20·5, t, C5; 21·4, t, C6; 24·0, t, C7; 28·8, q, Me; 36·1, t, C4; 40·0, s, C1; 40·8, t, C3; 42·0, s, C3a; 50·3, d, C2; 55·1, d, C7a; 62·8, t, CH_2OH; 114·4, s, CN; 117·6, s, CN. Selective irradiation of the proton

† The descriptors α and β in parentheses, at the beginning of such names, denote relative stereochemistry.

signal at δ 2·23 caused collapse of the ^{13}C doublet at δ 55·1 to a singlet. E.i.m.s. *m/z* 218 (M, 11%), 203 (M−Me, 13), 200 (M−H_2O, 19), 187 (M−CH_2OH, 100), 160 (M−CH_2OH−HCN, 35), 95 (97).

Further elution gave *imino lactone* (22) (4·4 mg, 16%, see below).

Jones Oxidation of Hydrindane (21) and Its Diastereoisomers

A mixture of hydrindane (21) and its diastereoisomers was prepared from epoxides (17)–(20) as described above. A solution of this mixture (43 mg) in acetone (1 ml) was cooled to 0°. Jones reagent (2·7 M CrO_3, 8 drops) was added over 2 h as the mixture was warmed to 20°. After a further hour, excess propan-2-ol was added followed by water and ethyl acetate (2 ml). The aqueous phase was separated and extracted twice with ethyl acetate. The combined organic layers were extracted with sodium bicarbonate solution (7%). The aqueous layer was cooled and acidified with 4 M hydrochloric acid and the mixture extracted with ethyl acetate (3×2 ml). The combined organic extracts were washed with saturated sodium bicarbonate solution, dried (Na_2SO_4) and evaporated to give a mixture of (23) and its diastereomeric acids as a crystalline solid (29 mg). ^1H n.m.r. δ [$(CD_3)_2CO$, $(CD_3)_2SO$, D_2O] 1·20, s, Me; 1·1–2·5, m; 3·42, dd, *J* 11·3, 9·5 Hz, C**H**COOH. E.i.m.s. *m/z* 232 (M, 15%).

Imino Lactone (22) from Epoxide (18)

A solution of epoxide (18) (43·1 mg, 0·20 mmol) in dry tetrahydrofuran (1·0 ml) was added to a stirred suspension of sodium hydride (10 mg, 55% oil dispersion, washed once with tetrahydrofuran, 0·23 mmol) under nitrogen. The pale yellow solution was stirred for 16 h. Ice-water and salt were added and the mixture was extracted with ether (3×5 ml). The combined ether extracts were washed with sodium bicarbonate solution (7%), dried ($MgSO_4$) and evaporated to give a colourless oil of *imino lactone* (22) (37 mg, 86%). Chromatography (m.p.l.c., 1 : 13 ethyl acetate/dichloromethane) gave an analytical sample of (22) which migrated as a single spot on t.l.c. (R_F 0·45, 1 : 9 ethyl acetate/dichloromethane) (Found: C, 71·6; H, 8·3. $C_{13}H_{18}N_2O$ requires C, 71·5; H, 8·3). ν_{max} (neat) 3300 (NH), 2240, 1690 cm^{-1} (C=NH). ^1H n.m.r. δ 0·76–2·1, m, 10H; 1·28, s, Me; 2·28, dd, *J* 12·4, 5·6 Hz, H 7aα; 3·55, qd, *J* 9·2, 4·4 Hz, OCH_2C**H**; 3·97, dd, *J* 9·2, 4·4 Hz, 1H, **H**CHO; 4·52, t, *J* 9·2 Hz, 1H, HC**H**O; 7·4, br s, 1H, C=NH. Irradiation of δ 4·52 caused partial collapse of 3·97 and 3·55. Irradiation of each of these in turn caused partial collapse of the other two but not δ 2·28. ^{13}C n.m.r. 21·52, t, 24·97, t, 25·55, t, C 5,6,7; 29·87, q, Me; 35·30, d, C 7a; 42·25, t, C 4; 46·14, s, C 1; 46·87, t, C 3; 53·0, s, C 3a; 54·43, d, C 2; 75·19, CH_2O; 122·17, s, CN; 167·81, s, C=NH. E.i.m.s. *m/z* 219 (M+1, 24%), 218 (M, 4), 203 (M−Me, 11), 122 (83), 109 (100). C.i.m.s. *m/z* 219 (M+1, 100%), 122 (9), 109 (11).

The same product was obtained when cyclization of (18) was attempted with one of several other bases (e.g. LiBr, KNH_2/NH_3, K_2CO_3/MeOH, $NaOCMe_2C_2H_5$/benzene, $KOBu^t$/dimethylformamide, triethylamine/toluene).

(1′R,2′S*,2″R*)-[2′-(3″-Bromo-2″-hydroxypropyl)-2′-methylcyclohexyl]propanedinitrile (24)*

A solution of hydrogen bromide in acetic acid (45% w/v, 0·15 ml, 0·84 mmol) was added over 5 min to a stirred solution of epoxide (17) (152 mg, 70% pure, 0·49 mmol) under nitrogen at −30°. After 15 min, dichloromethane (5 ml) and saturated sodium bicarbonate solution (5 ml) were added and the layers separated. The aqueous layer was extracted with dichloromethane (2×10 ml) and the combined organic layers were washed with saturated sodium chloride solution, dried (Na_2SO_4) and the solvent was removed to give a colourless oil (0·23 g) which was purified (m.p.l.c., 1 : 9 ethyl acetate/dichloromethane) to give pure *bromohydrin* (24) as a viscous, colourless oil (104 mg, 71%) (Found: $M^{+\bullet}$, 298·0677. $C_{13}H_{19}{}^{79}BrN_2O$ requires 298·0681). ν_{max} ($CHCl_3$) 3570, 2250 cm^{-1}. ^1H n.m.r. δ 1·19, s, Me; 1·1–2·1, m, 11H; 2·41, dd, *J* 4·5, 1·1 Hz, OH; 3·38, dd, *J* 9·8, 7·9 Hz, 1H, H 3″$_a$; 3·47, dd, *J* 9·8, 3·6 Hz, H 3″$_b$; 3·94, m, H 2″; 4·27, d, *J* 2·5 Hz, $CH(CN)_2$. ^{13}C n.m.r. δ 21·26, t, C 4′; 23·86, d, **C**H(CN)$_2$; 24·88, d, C 5′ or C 6′; 25·14, d, C 6′ or C 5′; 27·59, d, Me; 36·44, s, C 2′; 37·29, t, C 3′; 37·58, t, C 1″; 41·11, t, C 3″; 49·64, d, C 1′; 67·95, d, C 2″; 112·85,

s, CN; 114·08, s, CN. E.i.m.s. *m/z* 300/298 (M, 2%), 219 (M−Br, 10), 205 (M−CH_2Br, 100), 176 (22), 161 (46), 95 (85).

Bromohydrin (24) was also obtained (60% after purification) from the reaction of (18) with lithium tetrabromonickelate(II) (cf. below).

(1′R,2′R*,2″S*)-[2′-(3″-Bromo-2″-hydroxypropyl)-2′-methylcyclohexyl]propanedinitrile (26)*

A solution of dilithium tetrabromonickelate(II) (0·25 M, 2·5 ml, 0·53 mmol) in dry tetrahydrofuran was added dropwise to a stirred solution of epoxide (19) in dry tetrahydrofuran (4 ml) at 0° under nitrogen. The clear deep blue solution was stirred at 24° for 3 h during which time the colour changed to emerald green and back to blue. Aqueous sodium dihydrogen phosphate (10% w/v) was added to the stirred, cooled mixture until the colour was discharged. Dichloromethane (20 ml) and water (5 ml) were added and the layers separated. The aqueous phase was extracted with dichloromethane (2×5 ml) and the combined phases were washed with water (2×5 ml) and dried ($MgSO_4$). Removal of solvent and filtration through a short column of silica gave a crude *bromohydrin* (26) which was used without further purification. An analytical sample of (26) was obtained after two recrystallizations from n-hexane/dichloromethane, m.p. 106–107° (Found: C, 51·8; H, 6·4; N, 9·2. $C_{13}H_{19}BrN_2O$ requires C, 52·2; H, 6·4; N, 9·4%). ν_{max} (neat) 3200–3650, 2250 cm^{-1}. ^1H n.m.r. δ 1·05, s, Me; 1·1–2·4, m, 11H; 2·68, t, *J* 2·4 Hz, OH; 3·33, dd, *J* 10·6, 8·2 Hz, 1H, H3″$_a$; 3·40, dd, *J* 10·6, 3·9 Hz, 1H, H3″$_b$; 4·00, m, 1H, H2″; 4·31, d, *J* 1·7 Hz, $CH(CN)_2$. ^{13}C n.m.r. δ 12·02, Me; 21·44, t, C5′; 24·61, d, **C**H(CN)$_2$; 24·94, t, C4′ or C6′; 25·90, t, C6′ or C4′; 37·02, s, C2′; 38·66, t, C3′; 40·65, t, C3″; 44·47, d, C1′; 46·25, t, C1″; 67·22, d, C2″; 112·88, s, CN; 114·46, s, CN. E.i.m.s. *m/z* 300/298 (M, 0·2%), 219 (M−Br, 2), 205 (M−CH_2Br, 98), 210 (15), 176 (12), 161 (100).

Preparation of Lithium Tetrabromonickelate(II)[16]

Dry tetrahydrofuran (30 ml) was added to a mixture of powdered, anhydrous lithium bromide (2·61 g, 30 mmol) and anhydrous nickel(II) bromide (3·28 g, 15 mmol) under nitrogen. The mixture was stirred at 24° for 2–3 days during which time the salts dissolved slowly, giving a deep blue solution of the complex salt (*c.* 0·5 M). A small amount of residual suspended solid was allowed to settle (2–4 h) before use. The solution could be stored in a sealed ampoule at room temperature without appreciable decomposition.

Preparation of Bromohydrin O-Trimethylsilyl Ethers (25), (27) and (35)–(38)

Trimethylsilylimidazole (0·55 mmol) was added to a stirred solution of bromohydrin (0·11 mmol) in dry tetrahydrofuran (1·5 ml) at 0° under nitrogen. The mixture was allowed to warm to 25° over 25 min and the solvent removed under vacuum. The residue was dissolved in a small quantity of dichloromethane/n-hexane (1 : 2) and filtered through a short column of silica, eluting with the same solvent to afford the corresponding *O*-trimethylsilyl ether in quantitative yield. *Bromohydrin O-trimethysilyl ether* (25), colourless oil. ^1H n.m.r. same as that of (24) except for δ 0·18, s, 9H, $OSiMe_3$; 4·02, m, 1H, C**H**$OSiMe_3$ and absence of OH. ^{13}C n.m.r. δ 0·00, q, $OSiMe_3$. E.i.m.s. *m/z* 357/355 (M−Me, 15%), 277 (M−CH_2Br, 100). *Bromohydrin O-trimethylsilyl ether* (27), colourless oil. E.i.m.s. *m/z* 357/355 (M−Me, 18%), 277 (M−CH_2Br, 100). *Bromohydrin O-trimethylsilyl ether* (35), colourless oil. ^1H n.m.r. δ 0·04, s, 9H, $OSiMe_3$; 0·88, s, Me. E.i.m.s. *m/z* 332/330 (M−Me, 19%), 266 (M−Br, 13), 252 (M−CH_2Br, 100). *Bromohydrin O-trimethylsilyl ethers* (36) and (38), 5 : 1 mixture, colourless oil. (Found: $M^{+\bullet}$−Me, 330·0900. $C_{14}H_{25}{}^{79}BrNOSi$ requires 330·0889). ν_{max} ($CHCl_3$) 2245, 1250, 850 cm^{-1}. E.i.m.s. *m/z* 332/330 (M−Me, 38%), 252 (100). *Bromohydrin O-trimethylsilyl ether* (37), colourless oil. E.i.m.s. *m/z* 332/330 (M−Me, 33%), 252 (100).

(3α,4aβ,8aβ)-4a-methyl-3-trimethylsilyloxyoctahydronaphthalene-1,1(2H)-dicarbonitrile (6)

Dry, powdered potassium carbonate (114 mg) was added to a stirred solution of *O*-trimethylsilyl ether (25) (33 mg, 0·09 mmol) and 18-crown-6 (0·5 mol%) in dry dichloromethane (1·0 ml). The mixture was heated at reflux for 5 h, cooled and filtered (Celite). The solvent

was removed under vacuum to give the *decalin* (6) as a pale yellow oil (25·7 mg, quantitative) which was shown to be pure (^{13}C and ^{1}H n.m.r.) except for a trace of crown ether (Found: $M^{+\bullet}$, 290·1807. $C_{16}H_{23}N_2OSi$ requires 290·1814). ν_{max} (neat) 2250, 1250, 870, 750 cm^{-1}. ^{1}H n.m.r. δ 0·16, s, 9H, $SiMe_3$; 1·18, s, Me; 1·2–2·1, m, 12H; 2·46, ddd, J 12·9, 3·6, 2·2 Hz, H2$_a$; 4·11, tt, J 10·1, 3·6 Hz, H3β. ^{13}C n.m.r. δ 0·00, q, $SiMe_3$; 19·8, t, C6; 20·56, t, C7; 23·74, t, C8; 29·32, q, Me; 33·14, t, C5; 34·72, s, C1 or C4a; 35·45, s, C4a or C1; 43·65, t, C2; 46·46, d, C8a, 47·62, t, C4; 63·21, d, C3; 116·77, s, CN; 117·50, s, CN. E.i.m.s. *m/z* 290 (M, 3%), 275 (M−Me, 100), 100 (11).

(3α,4aβ,8aα)-4a-Methyl-3-trimethylsilyloxyoctahydronaphthalene-1,1(2H)-dicarbonitrile (7)

Bromohydrin *O*-trimethylsilyl ether (27) was quantitatively cyclized, as described above. Chromatography (silica, 3 : 2 dichloromethane/n-hexane) provided pure *decalin* (7) which crystallized from n-hexane as colourless cubes, m.p. 88–92° (Found: C, 66·4; H, 9·1; N, 9·5. $C_{16}H_{23}N_2OSi$ requires C, 66·2; H, 9·0; N, 9·6%). ν_{max} ($CHCl_3$) 2250, 1252, 1090 cm^{-1}. ^{1}H n.m.r. δ 0·15, s, 9H, $SiMe_3$; 1·16, s, Me; 1·1–2·0, m, 12H; 2·61, ddd, J 13·1, 4·4, 2·1 Hz, H2$_a$; 4·07, tt, J 11·5, 4·4 Hz, H3β. ^{13}C n.m.r. δ 0·00, q, $SiMe_3$; 18·02, q, Me; 20·26, t, C6; 24·21, t, C7; 26·22, t, C8; 35·62, s, C1 or C4a; 36·41, s, C4a or C1; 43·30, t, C2 or C5; 43·95, C5 or C2; 49·64, t, C4; 50·05, d, C8a; 62·98, d, C3; 115·62, s, CN; 116·18, s, CN. E.i.m.s. *m/z* 290 (M, 0·4%), 275 (100), 248 (10), 100 (24).

Hydrolysis of Decalindicarbonitrile (6)

A stirred solution of (6) (25 mg, 0·09 mmol) and aqueous potassium hydroxide (2% w/v) in ethanol (1 ml) and water (1 ml) was heated at reflux under nitrogen for 21 h. The solution was cooled and the ethanol removed under vacuum. Water (10 ml) was added and the solution extracted with ether (2×10 ml). The aqueous phase was cooled to 0° and acidified (pH 2–3) with 4 M hydrochloric acid then rapidly extracted with ethyl acetate (3×5 ml). The combined ethyl acetate layers were washed with water (3×5 ml), dried (Na_2SO_4) and evaporated to give the crude *dicarboxylic acid* (12) as an oily crystalline solid (29 mg). A sample crystallized from ethyl acetate as colourless prisms, m.p. 222–230°. E.i.m.s. *m/z* 256 (M).

Crude (12) (26 mg) was dissolved in ethyl acetate (2 ml) and treated with an excess of ethereal diazomethane. After 24 h, excess diazomethane was removed under a stream of nitrogen to give crude *dimethyl ester* (39) as an oily crystalline solid (R_F 0·83, 1 : 4 ethyl acetate/dichloromethane).

A small sample (*c.* 0·5 mg) was dissolved in pyridine (0·2 ml) and treated with bis(trimethylsilyl)trifluoroacetamide overnight. G.l.c./m.s. (100–200° at 10°/min) revealed several components, the predominant (51%) peak being the *O*-trimethylsilyl ether (40) of the dimethyl ester (39). *m/z* 340 (M, <1%), 325 (M−Me, <1%), 311 (M−OMe, 67), 73 (Me_3Si, 100).

(E)-[2′-Methyl-2′-(prop-2″-enyl)cyclohexylidene]acetonitrile (28)

Diethyl cyanomethylphosphonate (6·00 g, 34 mmol) was added to a stirred suspension of freshly prepared sodium amide (1·32 g, 34 mmol) in dry tetrahydrofuran (30 ml) under nitrogen.[17] The mixture was stirred for 5 h and a solution of ketone (13) (1·29 g, 8·46 mmol) in tetrahydrofuran (50 ml) was added dropwise. The mixture was stirred overnight and the solvent removed under reduced pressure. Water (50 ml) was added and the mixture extracted with ether (2×50 ml). The combined ether layers were washed twice with water, dried (Na_2SO_4) and evaporated to give a light yellow oil (2·38 g). Chromatography (silica, dichloromethane) afforded *nitrile* (28) (1·39 g, 93%) as the *E* isomer which was distilled (bulb to bulb, 100°/0·1 mm Hg) to give a colourless oil (Found: C, 82·2; H, 9·9. $C_{12}H_{17}N$ requiress C, 82·2; H, 9·8%). ν_{max} (neat) 3070, 2210, 1637, 1612 cm^{-1}. ^{1}H n.m.r. δ (C_6D_6) 0·65, s, Me; 0·7–1·5, m, 6H; 1·69, dd, J 14·0, 7·3 Hz, H1″$_a$; 2·01, m, 2H, H1″$_b$ and H6′*ax*; 2·62, dt, J 14·3, 4·5 Hz, 1H, H6′*eq*; 4·66, s, 1H, CHCN; 4·90, m, 2H, H3″; 5·33, m, H2″. ^{13}C n.m.r. δ 21·34, t; 24·67, q, Me; 27·62, t; 30·25, t; 39·45, t; 42·11, t; 92·97, d, CHCN; 117·82, s, CN; 133·67, d, C2″; 172·19, s, C1′. E.i.m.s. *m/z* 175 (M, 19%), 160 (M−Me, 8), 134 (M−C_3H_5, 100), 107 (41).

cis/trans-[2′-Methyl-2′-(prop-2″-enyl)cyclohexyl]acetonitrile (29) and (30)

Magnesium turnings (6·1 g, 252 mmol) and a crystal of iodine were added to a solution of nitrile (28) (1·10 g, 6·29 mmol) in methanol (60 ml).[18] An exothermic reaction ensued after 1 h and the mixture was stirred with external cooling (*c.* 30°) for 5 h. The mixture was further cooled (ice bath) and hydrochloric acid (6 M, 100 ml) added over 30 min. After a further 30 min ether (30 ml) was added and the layers were separated. The aqueous phase was extracted with ether (2×70 ml) and the combined ether layers were washed with saturated sodium bicarbonate and saturated sodium chloride solutions. After drying and removal of solvent the residue was distilled (Kugelrohr, 110°, 110°–140°/0·1 mm Hg) to give a 5 : 2 mixture of *nitriles* (29) and (30), as a colourless oil (0·98 g, 89%). The mixture migrated as a single spot on t.l.c. (R_F 0·57, toluene) (Found: C, 81·1; H, 10·5. $C_{12}H_{19}N$ requires C, 81·3; H, 10·8%). ν_{max} (neat) 3070, 2240, 1635 cm^{-1}. ^1H n.m.r. (of major *cis* isomer) δ 0·94, s, Me; 2·10, dd, *J* 16·6, 10·1 Hz, 1H, CH**H**CN; 2·52, dd, *J* 16·6, 3·9 Hz, 1H, C**H**HCN; 5·07, m, 2H, $(H3'')_2$; 5·73, m, H2″. ^{13}C n.m.r. δ 18·6, t, $\mathbf{C}H_2CN$; 21·34, t, C4′; 25·34, t, C5′; 26·54, q, Me; 27·12, t, C6′; 35·59, s, C2′; 36·41, 2×t, C3′ and C1″; 44·30, d, C1′; 116·5, s, CN; 117·64, t, C3″; 133·88, d, C2″. [trans (30)] ^1H n.m.r. δ 0·82, s, Me.

Treatment of Olefins (29) and (30) with N-Bromosuccinimide: Bromohydrins (31)–(34)

N-Bromosuccinimide (0·56 g, 3·1 mmol) was added in one portion to a stirred mixture of nitriles (29) and (30) (5 : 2, 0·46 g, 2·6 mmol) in dioxan (10 ml) and water (8 ml). The mixture was heated (60°) for 3 h with stirring, cooled, poured into ice-water (20 ml), and extracted with dichloromethane (3×20 ml) and the combined organic layers were washed successively with water, aqueous solutions of sodium sulfite (0·5 ml), sodium bicarbonate and water. After drying (Na_2SO_4) the solvent was removed under vacuum to yield a pale yellow oil (0·8 g) which was subjected to m.p.l.c. (silica, 1 : 46 ethyl acetate/dichloromethane) to give, in order of elution: (i) an unidentified brown oil (*c.* 5 mg); (ii) a colourless oil (131 mg) *(1′R*,2′S*,2″R*)-[2′-(3″-bromo-2″-hydroxypropyl)-2′-methylcyclohexyl]acetonitrile* (31) (Found: $M^{+\bullet}$, 273·0698. $C_{12}H_{20}{}^{79}BrNO$ requires 273·0729). ν_{max} (neat) 3450, 2250 cm^{-1}. ^1H n.m.r. δ 1·02, s, Me; 0·9–1·93, m, 11H; 2·08, dd, *J* 16·7, 10·2 Hz, C**H**HCN, 2·48, dd, *J* 16·7, 3·7 Hz, CH**H**CN; 2·42, br s, OH; 3·39, dd, *J* 9·9, 6·7 Hz, 1H, $H3''_a$; 3·46, dd, *J* 9·9, 4·4 Hz, 1H, $H3''_b$; 3·88, m, H2″. ^{13}C n.m.r. δ 18·60, t, $\mathbf{C}H_2CN$; 21·60, t, C4′; 25·4, t, C5′; 27·00, q, Me; 27·09, t, C6′; 35·21, s, C2′; 36·20, t, C3′ or C1″; 36·96, t, C1″ or C3′; 41·66, t, C3″; 45·34, d, C1′; 68·00, d, C2″; 119·80, s, CN. C.i.m.s. *m/z* 293/291 ($M+NH_4$, 44%), 276/274 (MH, 10), 258/256 ($MH-H_2O$, 22), 136 (100). E.i.m.s. *m/z* 275/273 (M, <0·2%), 258/256 ($MH-H_2O$, 0·7%), 194 (M−Br, 21), 180 ($M-CH_2Br$, 46), 136 (100); (iii) a low melting solid (14 mg), *(1R*,2R*,2′S*)-[2′-(3″-bromo-2″-hydroxypropyl)-2′-methylcyclohexyl]acetonitrile* (33) (Found: $M^{+\bullet}$, 273·0722. $C_{12}H_{20}{}^{79}BrNO$ requires 273·0729). ν_{max} ($CHCl_3$) 3560, 2250 cm^{-1}. ^1H n.m.r. δ 0·84, s, Me; 1·2–2·0, m, 11H; 1·98, m, 1H, C**H**HCN; 2·32, br s, OH; 2·70, m, 1H, CH**H**CN; 3·33, dd, *J* 10·2, 7·8 Hz, $H3''_a$; 3·42, dd, *J* 10·2, 3·9 Hz, $H3''_b$; 3·98, m, H2″. ^{13}C n.m.r. δ 19·42, t, $\mathbf{C}H_2CN$; 19·59, q, Me; 21·78, t, C4′; 25·84, t, C5′; 27·68, t, C6′; 36·00, s, C2′; 37·84, t, C3′; 40·06, d, C1′; 41·73, t, C3″; 46·46, t, C1″; 67·51, d, C2″; 120·30, s, CN. E.i.m.s. *m/z* 275/273 (M, 0·1%), 258/256 (M−Me, 0·4), 215 (2), 194 (M−Br, 4), 180 ($M-CH_2Br$, 30), 136 (100), 95 (74); (iv) a mixed fraction containing *bromohydrins* (32) and (34) (31 mg); (v) a colourless oil (215 mg), identified as an inseparable 5 : 1 mixture of *(1′R*,2′S*,2″S*)-[2′-(3″-bromo-2″-hydroxypropyl)-2′-methylcyclohexyl]acetonitrile* (32) and its C1′ *epimer* (34) (Found: $MH^{+\bullet}-H_2O$, 256·0699. $C_{12}H_{19}{}^{79}BrN$ requires 256·0701). ν_{max} (neat) 3560, 2250 cm^{-1}. ^1H n.m.r. [major isomer (31)] δ 1·10, s, Me; 1·0–2·0, m, 11H; 2·13, dd, *J* 16·6, 10·5 Hz, C**H**HCN; 2·62, dd, *J* 16·6, 3·7 Hz, CH**H**CN; 2·39, br s, OH; 3·37, dd, *J* 10·2, 7·1 Hz, $H3''_a$; 3·46, dd, *J* 10·2, 4·2 Hz, $H3''_b$; 3·89, m, H2″. ^{13}C n.m.r. δ 18·48, t, $\mathbf{C}H_2CN$; 21·67, t, C4′; 24·94, t, C5′; 26·89, t, C6′; 27·33, q, Me; 36·62, t, C3′ or C1″; 37·05, t, C1″ or C3′; 41·58, t, C3″; 44·67, d, C1′; 67·83, d, C2″; 120·0, s, CN. E.i.m.s. *m/z* 276/274 (MH, 0·7%), 258/256 ($MH-H_2O$, 5), 194 (M−Br, 12) 180 ($M-CH_2Br$, 56), 136 (100). C.i.m.s. *m/z* 291 ($M+NH_4$, 100), 256 ($MH-H_2O$, 24). [Epimer (34)] ^1H n.m.r. δ 0·93, s, Me. ^{13}C n.m.r. δ 46·84, t, C3″; 67·57, d, C2″; (vi) a pale yellow oil (48 mg) comprising a mixture of compounds which were not identified.

The combined yield of bromohydrins was 391 mg (55%).

Cyclization of O-Trimethylsilyl Ethers (35)–(38): Decalincarbonitriles (8)–(11)

The preparation of decalincarbonitriles is exemplified by the following procedure for the synthesis of (9) and (11). A freshly prepared solution of lithium hexamethyldisilazide (0·83 M, 2·3 ml, 1·9 mmol) in tetrahydrofuran/n-hexane was added to a stirred solution of (36) and (38) (5 : 1, 220 mg, 0·64 mmol) in dry tetrahydrofuran (5 ml) at −30° under nitrogen. After 0·5 h cold aqueous potassium phosphate buffer (10% w/v, pH 7, 10 ml) and dichloromethane (20 ml) were added. The layers were separated and the aqueous phase was extracted with dichloromethane (×2). The combined organic layers were washed with saturated aqueous sodium chloride (×2), dried (Na_2SO_4) and evaporated to give a straw coloured oil (170 mg, quantitative). This was subjected to chromatography (silica, 1 : 1 dichloromethane/hexane) to give two fractions, in the following order of elution. (i) *(1ξ,3α,4aα,8aβ)-4a-Methyl-3-trimethylsilyloxydecahydronaphthalene-1-carbonitrile* (11), a colourless oil (43 mg), comprising a 1 : 1 mixture of C1 epimers (Found: $M^{+\bullet}$, 265·1867. $C_{15}H_{27}NOSi$ requires 265·1862). ν_{max} ($CHCl_3$) 2240, 1250, 1155, 840 cm^{-1}. ^1H n.m.r. δ 0·05, s, 9H, $SiMe_3$; 1·00, s, Me; 2·73, m, 0·5 H, H1*eq*; 3·38, dt, *J* 12·4, 3·9 Hz, 0·5 H, H1*ax*; 4·07, m, $W_{h/2}$ 9·5 Hz, 1H, H3*β*. ^{13}C n.m.r. δ 18·05, q, Me; 66·11, 66·17, 2×d, C3; 122·61, 123·00, 2×s, CN. E.i.m.s. *m/z* 265 (M, 6%), 250 (M−Me, 100). 155 (45), 75 (62). (ii) *(1α,3α,4aα,8aα)-4a-Methyl-3-trimethylsilyloxydecahydronaphthalene-1-carbonitrile* (9), a colourless oil (91 mg) (Found: $M^{+\bullet}$, 265·1867. $C_{15}H_{27}NOSi$ requires 265·1862). ν_{max} ($CHCl_3$) 2240, 1265, 1090, 875, 840 cm^{-1}. ^1H n.m.r. δ 0·06, s, $SiMe_3$; 1·01, s, Me; 1·0–1·8, m, 12H; 2·20, m, 1H; 2·81, td, *J* 12·7, 3·4 Hz, H1*β*; 3·69, tt, *J* 11·2, 4·4 Hz, H3*β*. Irradiation of the methyl group did not give detectable n.O.e. to H1*β* or H3*β*. ^{13}C n.m.r. δ 0·14, q, $SiMe_3$; 19·88, t, C6; 21·52, t, C7; 24·08, t, C8; 27·64, d, C1; 28·08, q, Me; 31·27, t, C5; 34·27, s, C4a; 39·24, t, C2; 42·89, d, C8a; 50·00, t, C4; 65·25, d, C3; 121·61, s, CN. E.i.m.s. *m/z* 265 (M, 0·8%), 250 (M−Me, 100), 149 (23). The combined isolated yields of decalins (9) and (11) was 134 mg (80%). Decalins (8) and (10) were prepared in a similar manner.

O-Trimethylsilyl ether (37) (13·7 mg, 0·04 mmol) gave *(1α,3α,4aβ,8aα)-4a-methyl-3-trimethylsilyloxydecahydronaphthalene-1-carbonitrile* (10), a colourless oil (11 mg, 100%) (Found: $M^{+\bullet}$−Me, 250·1624. $C_{14}H_{24}NOSi$ requires 250·1627). ν_{max} ($CHCl_3$) 2240 cm^{-1}. ^1H n.m.r. δ 0·08, s, $SiMe_3$; 0·81, s, Me; 1·1–1·9, m, 12H; 2·23, m, 1H; 2·36, td, *J* 12·6, 3·6 Hz, H1*β*; 3·77, tt, *J* 11·2, 4·6 Hz, H3*β*. Irradiation of the methyl signal (δ 0·81, s) gave rise to significant n.O.e. of H1*β* (8%) and H3*β* (14%). ^{13}C n.m.r. δ 0·02, s, $SiMe_3$; 16·81, Me; 20·73, t, C6; 25·54, t, C7 or C8; 26·36, t, C8 or C7; 30·42, d, C1; 34·65, s, C4a; 39·71, t, C2; 41·31, t, C5; 46·80, d, C8a; 50·48, t, C4; 65·43, d, C3; 121·40, s, CN. E.i.m.s. *m/z* 265 (M, 3%), 250 (M−Me, 100), 232 (99), 173 (71).

O-Trimethylsilyl ether (35) (57 mg, 0·16 mmol) gave *(1α,3α,4aβ,8aβ)-3-hydroxy-4a-methyldecahydronaphthalene-1-carbonitrile* (8) (20 mg, 63%), which crystallized from ether/n-hexane as colourless prisms, m.p. 100–102° (Found: C, 74·2; H, 9·9; N 7·3. $C_{12}H_{19}NO$ requires C, 74·6; H 9·9; N, 7·3%). ν_{max} ($CHCl_3$) 3700–3300, 2240, 1090 cm^{-1}. ^1H n.m.r. δ 0·97, s, Me; 1·1–1·9, m, 12H; 2·10, m, 1H, $H2_a$; 3·07, dt, *J* 13·5, 3·3 Hz, H1*β*; 3·90, tt, *J* 11·2, 4·7 Hz, H3*β*. Irradiation of the methyl signal (δ 0·97, s) gave significant n.O.e. of H3*β* (3%) and H1*β* (5%). ^{13}C n.m.r. δ 21·55, t, C6; 23·18, t, C7; 26·08, t, C8; 28·27, d, C1; 28·44, q, Me; 32·85, t, C2; 34·63, s, C4a; 38·37, t, C4; 40·97, t, C5; 42·16, d, C8a; 66·20, d, C3; 122·0, s, CN. E.i.m.s. *m/z* 193 (M, 0·7%), 175 (M−H_2O, 16), 160 (41), 133 (39), 109 (55), 95 (100).

Hydrolysis of Nitrile (9)

Potassium hydroxide solution (40% w/v, 3 ml) was added to a stirred solution of (9) (76 mg, 0·29 mmol) in ethanol (3 ml) under nitrogen. After heating the mixture at reflux for 6 h the ethanol was removed under reduced pressure and the aqueous solution diluted with water (15 ml) and extracted with ether. The ether extracts were washed with water (15 ml) and extracted with ether. The combined ether extracts were washed with water, dried (Na_2SO_4) and evaporated to give a colourless solid (11·8 mg). The aqueous phase was acidified (6 M HCl) and extracted with ethyl acetate (3×10 ml). The extracts were combined, washed, dried and evaporated as before to give an almost colourless solid (30 mg). Reextraction of the washings gave additional solid (17 mg). T.l.c. showed these three solids to be the

same compound, *(1α,3α,4aα,8aα)-3-hydroxy-4a-methyldecahydronaphthalene-1-carboxamide* (41) (combined, 58 mg, 86%). Crystallization from ethyl acetate afforded colourless plates, m.p. 200–202° (Found: C, 68·5; H, 10·2; N, 6·4. $C_{12}H_{21}NO_2$ requires C, 68·2; H, 10·0; N, 6·6%). ν_{max} (Nujol) 3400–3200, 1655, 1620 cm^{-1}. ^1H n.m.r. δ [$(CD_3)_2CO$] 1·03, s, Me; 0·9–1·9, m; 2·71, m, H1β; 3·62, br s, OH; 3·75, m, H3β; 6·23, 6·85, 2×br s, 2H, NH_2. E.i.m.s. *m/z* 211 (M, 12%), 95 (12), 94 (13), 72 (100), 55 (11).

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