Synthesis of 4,4-Disubstituted Cyclohexenones. Part 3.† The Reaction of 1,3-Bis(trimethylsilyloxy)cyclohexa-1,3-dienes with Dienophiles. An Unexpected Rearrangement of the Adducts from the Reaction with 2-Chloroacrylonitrile

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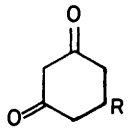
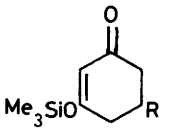
The cycloaddition of 2-chloroacrylonitrile to 1,3-bis(trimethylsilyloxy)cyclohexa-1,3-dienes (**3**) occurs in good yield to give after base-catalysed silyl enol ether cleavage the adducts (**4**). Cycloaddition with acrylonitrile occurs in moderate yield, while more reactive dienophiles such as nitroethylene and *E*-nitroacrylate lead to adducts which rapidly rearrange or decompose. The cycloaddition of 2-chloroacrylonitrile to diene (**3b**) in toluene, hexane, or dichloromethane in the presence of Lewis acids such as Me_2AlCl or $TiCl_4$ occurs in high yield at −78 °C with great *syn*-selectivity and a slight preference for the *exo*-nitrile stereochemistry. Desilylation of adducts (**4a**) and (**4b**) gave respectively the alcohols (**8a**) and (**8b**) and the novel bicyclic ether rearrangement products (**9a**) and (**9b**) whose yield could be maximised by carrying out the desilylation with Bu_4NF in the presence of 4 Å molecular sieves. The diols (**14a**) and (**14b**) prepared by borohydride reduction of ketones (**4**) did not undergo this rearrangement thereby confirming that the presence of the carbonyl group in (**4**) was essential. Borane–THF reduction of the alkoxyenones (**9**) caused the unexpected formation of the cyclohexenes (**15**). Lewis acid-catalysed cycloaddition of 2-chloronitrile to the methoxysilyloxydiene (**16a**) gave the adduct (**17**) in moderate yield with concomitant formation of rearrangement products (**18**) and (**19**). The corresponding addition to (**16b**) was not promising.

The reaction of 1,3-dimethoxycyclohexa-1,4-dienes with 2-chloroacrylonitrile had not proved an expedient route to 5-oxobicyclo[2.2.2]octane-2-carbonitriles (see Part 2, this series) as the *endo*-adducts initially formed rearranged too easily to the bicyclo[3.2.1] system. Additionally the stereoselectivity of the cycloaddition was low when the diene contained only small substituents on the ethano-bridge. Our first attempts to improve the reaction by using a double Michael reaction[1] to generate the bicyclic system did not succeed. A report by Inubushi[2] suggested to us that the use of bis-silyloxycyclohexadienes instead of the dimethoxydienes might lead to higher yields of the required adducts under milder conditions.

The required dienes (**3a**) and (**3b**) could be prepared by either of two methods; the first method, that of Simchen,[3] allowed direct preparation of the dienes (**3a**) and (**3b**) in nearly quantitative yield, from the diones (**1a**) and (**1b**) respectively, by reaction of the latter with trimethylsilytrifluoromethane sulphonate and triethylamine; the second method, due to Ainsworth, was more suitable for large-scale reactions. Reaction of the cyclohexanediones (**1a**) and (**1b**) with hexamethyldisilazane and imidazole[4] gave the enones (**2a**) and (**2b**) respectively in 95% yield. Treatment of the enones (**2a**) and (**2b**) with lithium hexamethyldisilazide followed by chlorotrimethylsilane then gave the dienes (**3a**) and (**3b**) in 90% yield.[5]



(**1**) **a**; R = H
b; R = Me



(**2**) **a**; R = H
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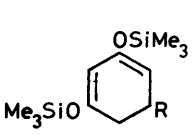
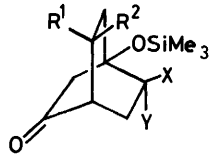


(**3**) **a**; R = H
b; R = Me



(**4**)

a; $R^1 = R^2 = H$, X = CN, Y = Cl
b; $R^1 = R^2 = H$, X = Cl, Y = CN
c; $R^1 = R^2 = H$, X = CN, Y = H
d; $R^1 = R^2 = H$, X = H, Y = CN
e; R^1 = Me, $R^2 = H$, X = CN, Y = Cl
f; R^1 = Me, $R^2 = H$, X = Cl, Y = CN
g; $R^1 = H$, R^2 = Me, X = CN, Y = Cl
h; $R^1 = H$, R^2 = Me, X = Cl, Y = CN

When the diene (**3a**) was caused to react with 2-chloroacrylonitrile at 65 °C a 65% yield of the adducts (**4a**) and (**4b**) was obtained in a 10:1 ratio after hydrolysis of the intermediate silyl enol ether with methanolic K_2CO_3.[6] Further investigation of this reaction demonstrated that it proceeded rapidly even at room temperature. Under these conditions the adducts were obtained in 97% yield as a 1.1–1.2:1 mixture of isomers. It is presumed that the adduct (**4b**) is formed in high yield at 65 °C, but that it is removed by rearrangement to the bicyclo-[3.2.1]system.

The reaction of the diene (**3a**) with several other dienophiles was examined. With acrylonitrile the adducts (**4c**) and (**4d**) were formed in 44% yield after 28 days at room temperature, while after reaction at 65 °C over 2 days the yield was 61%. In both cases the ratio of adducts was about 1:1. With the more reactive dienophiles nitroethylene[7] and *E*-3-nitro acrylate[8] the Diels–Alder adducts could not be isolated. In the former case the retro-aldol product, the dione (**5**), was isolated in 81% yield, while in the latter the adducts (**6**) could only be

† Part 2. Preceding paper. Preliminary Communication R. S. J. Clark, A. B. Holmes, and V. G. Matassa, *Tetrahedron Lett.*, 1989, **30**, 3223.
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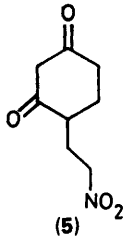
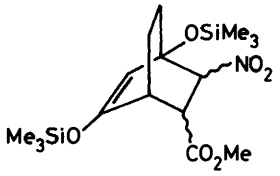
Table The Lewis acid-catalysed addition of 2-chloroacrylonitrile to the diene (**3b**) in various solvents

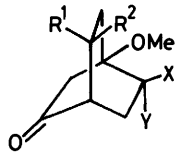
Lewis acid	Solvent	Yield (%) of [2.2.2] adduct (**4**)	Ratio *syn/anti* (**4e, f**):(**4g, h**)	*Exo/endo* ratio for *syn*-isomer (**4e**):(**4f**)
$TiCl_4$	CH_2Cl_2	12	>40:1	2:1
$TiCl_4$	Hexane	62	>20:1	2.5:1
$TiCl_4$	Toluene	49	>25:1	4:1
Me_2AlCl	CH_2Cl_2	33	>20:1	2:1
Me_2AlCl	Hexane	100	>20:1	10:7
Me_2AlCl	Toluene	100	>25:1	4:1



(**5**)



(**6**)



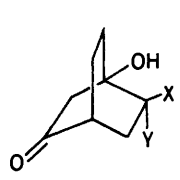
(**7**) **a**; R^1 = Me, R^2 = H, X = CN, Y = Cl
b; R^1 = Me, R^2 = H, X = Cl, Y = CN
c; R^1 = H, R^2 = Me, X = CN, Y = Cl
d; R^1 = H, R^2 = Me, X = Cl, Y = CN

identified as a crude reaction product, but decomposed on all attempts to purify them or to convert the enol ether into a ketone.

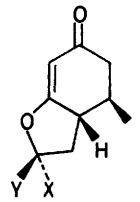
When the diene (**3b**) reacted with 2-chloroacrylonitrile in toluene at 65 °C, a mixture of the adducts (**4e–h**) was obtained in 53% yield. Comparison of the ^1H NMR spectrum of this mixture with those of the very similar compounds (**7a**), (**7b**) and (**7c**) showed that the *syn* to *anti* methyl ratio of the mixture was approximately 3:1, *i.e.* almost exactly the same as in the corresponding reaction of 1,3-dimethoxy-5-methylcyclohexa-1,4-diene with 2-chloroacrylonitrile (see preceding paper). When the diene (**3b**) and 2-chloroacrylonitrile were allowed to react at room temperature the adducts (**4e–h**) were obtained in a 10:7:1.2:1 ratio, as determined by ^1H NMR and GC, *i.e.* an overall *syn*:*anti* ratio of 8:1, and in a yield of 80% after hydrolysis of the enol ether.

In order further to improve this reaction the effect of stoicheiometric quantities of Lewis acids on the yield and selectivity of the cycloaddition of (**3b**) to 2-chloroacrylonitrile was examined (Table). The reactions were run at low temperature (in a solid CO_2–acetone bath) overnight, and were then quenched. When THF was used as the solvent none of the Lewis acids used ($BF_3 \cdot OEt_2$, $ZnCl_2$, ZnI_2, CF_3CO_2H, $TiCl_4$, $AlCl_3$, $Me_3SiOSO_2CF_3$, $Zr(OPr^i)_4$, $Ti(OPr^i)_4$, Me_2AlCl, Me_3Al) was effective, and a number of unidentified products were obtained. In the other solvents used (hexane, toluene, dichloromethane) both the Lewis acids tried ($TiCl_4$,Me_2AlCl) gave a remarkably high *syn*:*anti* ratio, and a small *exo* (nitrile) selectivity. In all these cases the reaction was clean, and in the first four cases the bulk of remaining mass was accounted for by 5-methylcyclohexane-1,3-dione (**1b**), which implies the reaction had not yet gone to completion. The catalytic effect of Me_2AlCl is noteworthy especially in view of the recently observed asymmetric induction with chiral aluminium binaphthyl catalysts.[9]

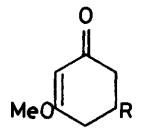
In order to use the adducts (**4a**), (**4b**), (**4e**), and (**4f**) in our synthesis of cyclohexenones it was deemed necessary to convert



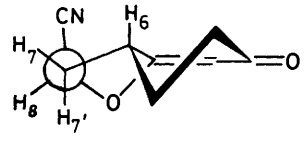
(**8**) **a**; X = CN, Y = Cl
b; X = Cl, Y = CN



(**9**) **a**; R = H, X = CN, Y = H
b; R = H, X = H, Y = CN
c; R = Me, X = CN, Y = H
d; R = Me X = H, Y = CN



(**10**) **a**; R = H
b; R = Me



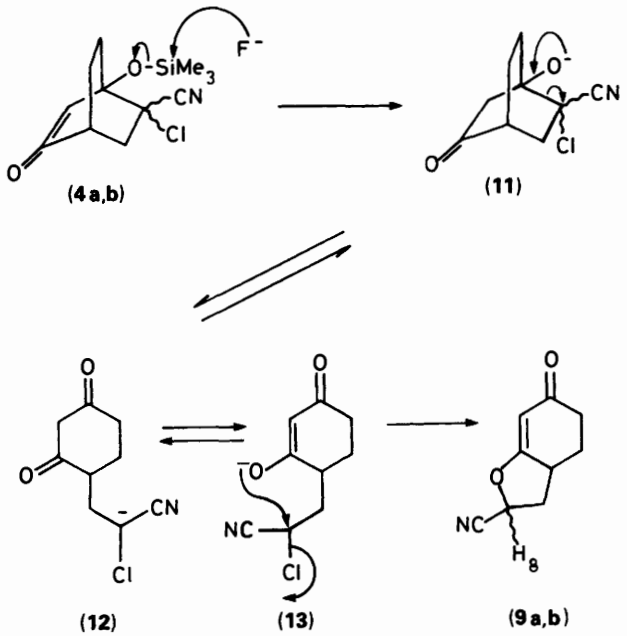
(**9b**)

Figure 1.

the chloronitrile to a ketone in order that the Baeyer–Villiger strategy could be employed. It was expected that the silyl ether of these adducts would not be stable to the sodium sulphide/potassium hydroxide/95% ethanol,[10] or the potassium hydroxide/DMSO[11] hydrolysis conditions. In any case reaction of the mixture of adducts (**4a**) and (**4b**) under either of these conditions did not give the required diketone. It was decided to convert the silyl ether into a base-stable alcohol derivative, and with this in mind the mixture of adducts (**4a**) and (**4b**) was treated with *tetra*butylammonium fluoride in THF[12] to effect deprotection of the alcohol. Under these conditions a 55% yield of the alcohols (**8a**) and (**8b**) was isolated, and in addition two, unexpected, ultra-violet absorbing compounds were formed. These were assigned the structure (**9a**) (less polar, 9%) and (**9b**) (more polar, 12%), on the basis of their spectral characteristics. A series of decoupling experiments, and comparison of the ^{13}C NMR spectra of (**9a**) and (**9b**) with those of (**10a**) and (**10b**) corroborated this deduction.

The relative stereochemistry between C-6 and C-8 was assigned on the basis of the coupling constants between the proton on C-8 and the protons of the neighbouring methylene group. If the enone is flat to allow for the best orbital overlap, then when H_6 and H_8 are on different faces of the five-membered ring, *i.e.* (**9b**), one of the protons (H_7) of the neighbouring methylene group is orthogonal to H_8 (Figure 1). It would therefore be expected to have either a very small coupling, or none at all, to H_8. The latter is in fact the case in the more polar isomer (**9b**), where H_8 appears as a doublet (vicinal coupling to $H_{7'}$, J 8.4 Hz) while in the less polar isomer (**9a**) H_8 appears as a double doublet (vicinal coupling 11.1, 5.7 Hz to $H_{7,7'}$).

A possible mechanism for this transformation is outlined in Scheme 1. Initial desilylation of the adducts would give the alkoxide anion (**11**). This would be in equilibrium with the cleavage product (**12**) in which the charge is stabilised by the neighbouring nitrile and chlorine. This possibly unfavourable equilibrium could be driven over by removal of one of the acidic protons between the carbonyl groups of the dione (**12**) in an intra-or inter-molecular proton transfer to give the enolate anion (**13**). This can now cyclise by displacement of the activated chloride by the enolate oxygen. From this mechanism one can draw three inferences; firstly the diastereoisomeric ratio of the product will be independent of that of the starting material, as it is determined by the protonation of the anion in

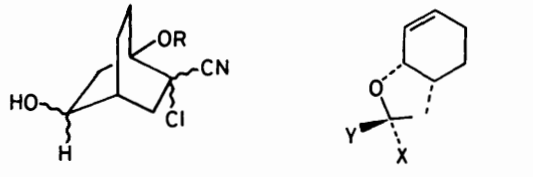


Scheme 1.

the step (12) → (13); secondly the presence of the carbonyl group in the starting material is necessary to drive the equilibrium over to the open form (13); lastly the reaction will be dependent on the nature of the cation, as a cation that is too closely associated with the alkoxide (11) or the anion (13) would inhibit the reaction.

The first deduction could be verified easily as reaction of the single isomer (**4a**) obtained by two fractional recrystallisations of the 10:1 mixture of isomers, or reaction of the mixture of isomers (**4a, b**) from the Diels–Alder reaction at 65 °C, gave the same ratio of products (**9a**) and (**9b**).

The diols (**14a**) could be prepared by reduction of the ketones (**4a, b**) ($NaBH_4$, room temp., 78%), and the alcohols (**14b**) could be prepared similarly ($NaBH_4$, 0 °C, 56%). Neither of these could be induced to undergo a cleavage of the C(1)–C(2) bond under treatment with base (2 equiv. KH), or when the alkoxide was generated from the ether (Bu_4NF), confirming the need to have a carbonyl group in the starting material.



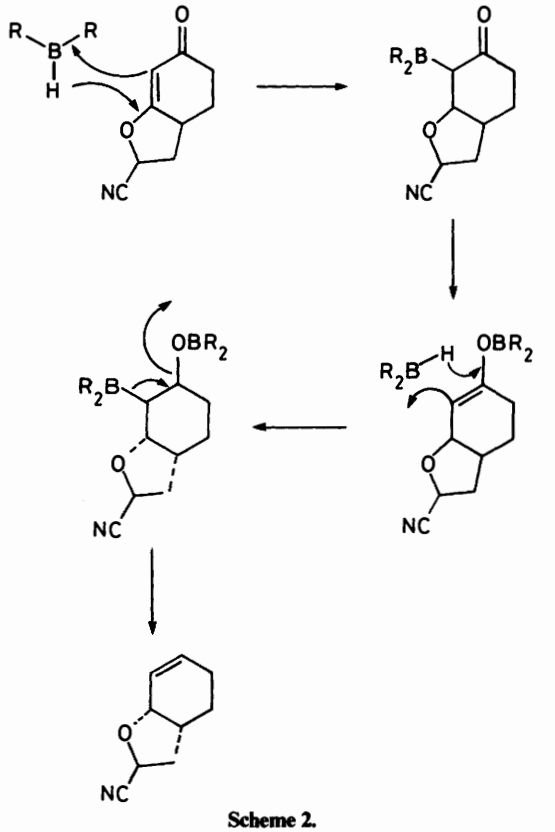
(**14**) **a**; R = H
b; R = Me_3Si

(**15**) **a**; X = CN
b; X = H, Y = CN

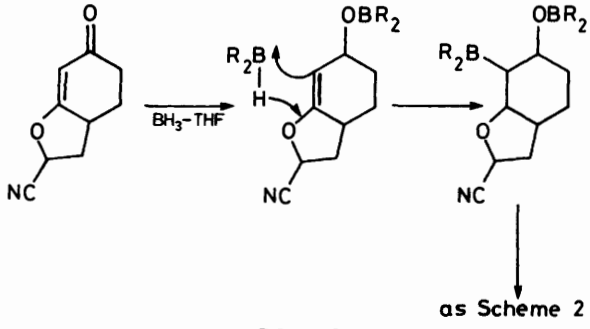
Attempts to generate the anion (**11**) from the alcohols (**8a, b**) under a variety of conditions (K_2CO_3, NaH, KH, Et_3N, DBU or KF in CH_3CN) did not lead to any reaction. Reaction of (**8a, b**) with Bu_4NF led to a low conversion to the rearranged products. With 1.1 equiv. NaH and Bu_4NF a 39% conversion into the rearranged products was observed. Treatment of the mixture of adducts (**4a, b**) with K_2CO_3/MeOH simply led to conversion into the alcohols (**8a, b**) in 95% yield. It therefore appears that the success of the reaction is strongly dependent on the method used to generate the alkoxide anion (**11**). The best method for obtaining a high yield of the rearrangement products involves reaction of the Diels–Alder adducts with Bu_4NF in the presence of 4 Å molecular sieves. In this way a 49–89% yield of the products (**9a, b**) can be obtained. Treatment of the adducts (**4e, f**) under these conditions gave the bicyclo-[4.3.0] systems (**9c, d**) in 42% combined yield and in a 1:1 ratio.

If a nucleophile could be added in a Michael reaction to the double bond of the enones (**9**), or if the double bond could be reduced, an extremely direct route to cyclohexenone derivatives would have been developed. Unfortunately despite extensive experimentation conjugate addition to these systems has only been achieved in very low yield. It is likely that the recently discovered *in situ* addition of organocuprates to enones in the presence of Me_3SiCl will overcome this difficulty.[13] The reaction of the isomer (**9a**) with borane–NHF at solid CO_2–acetone temperature gave the alkene (**15a**) in 70% yield. Under the same conditions the isomer (**9b**) gave the alkene (**15b**) in 30% yield, with 40% recovery of starting material. Two possible mechanisms for this transformation are outlined in Schemes 2 and 3.

The Lewis acid catalysed cycloaddition has been extended to the reaction of 1-methoxy-3-silyloxycyclohexa-1,3-dienes. Thus the diene (**16a**; R=H), prepared from 3-methoxycyclohex-2-

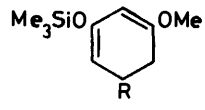


Scheme 2.

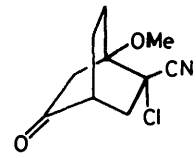


Scheme 3.

enone (LDA then TMSA, 80%) reacted with 2-chloroacrylonitrile at 70 °C for 1 h to give, after base hydrolysis of the enol ether, the adduct (**17**) (38%), the rearranged product (**18**) (14%), and the tricyclic system (**19**) (15%). When the reaction was performed at room temperature after one week the yield of (**17**), (**18**), and (**19**) were 14%, 4% and 23% respectively, while 3-methoxycyclohexenone was recovered. This suggests that (**19**) is an intermediate in the formation of (**18**) and this was confirmed by heating (**19**) under the normal Diels–Alder reaction conditions when (**18**) was produced.

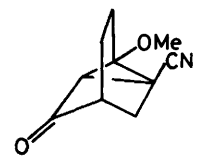


(**16**) **a**; R = H
b; R = CH_2OSiMe_3



(**17**)

(**18**)



(**19**)

In summary the use of 1,3-oxygen-substituted cyclohexa-1,3-dienes in the presence of Lewis acids has enabled the stereocontrolled and efficient synthesis of 8-substituted-5-oxabicyclo[2.2.2]octane-2-carbonitriles. When the diene contained two silyl enol ethers the Diels–Alder adducts could be arranged directly to the bicyclo[4.3.0]nonane systems *via* an unprecedented reaction.

Experimental

Apparatus and equipment are described in the preceding paper in this journal (Part 2).

1,3-Bis(trimethylsilyloxy)cyclohexa-1,3-diene (**3a**)[2] was prepared either by direct silylation of cyclohexane-1,3-dione (**1a**) with trimethylsilyl triflate,[3] or by conversion into the silyloxy cyclohexenone (**2a**) with hexamethyldisilazane and imidazole,[4] followed by further silylation (trimethylchlorosilane) of the lithium dienolate (generated with lithium hexamethyldisilazide).[5]

2-Chloro-5-oxo-1-trimethylsilyloxybicyclo[2.2.2]*octane-2-carbonitrile* (**4a, b**).—Diene (**3a**) (4.1 g, 16 mmol) and 2-chloroacrylonitrile (4.1 g) were stirred at room temperature for 20 h in dry dichloromethane (5 ml). The solvent was then evaporated under reduced pressure and the residues were dissolved in methanol (30 ml) containing potassium carbonate (0.17 g). The mixture was stirred for 1 h at 0 °C, then the solvent was evaporated under reduced pressure and the residues were partitioned between water (30 ml) and ethyl acetate (20 ml). The aqueous phase was extracted with ethyl acetate (2 × 30 ml) and the combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure to give an oil which was purified by passing through a short Florisil column (100 g), washing it through with ethyl acetate, and recrystallisation from ether of the solid which resulted when the filtrate was evaporated. This gave the *ketones* (**4a, b**) (4.2 g, 97%) as a white, crystalline solid, m.p. 68–70 °C; $\nu_{max}(CHCl_3)$ 2 950m, 2 250w, 1 730s, 1 600m, 1 320m, 1 160s, 885s, and 845s cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 2.97–3.06 (1 H, dd, *J* 18.5, 3.5 Hz, H_{6r}), 2.83–2.90 (1 H, dd, *J* 15.6, 2.8 Hz, H_{3r}), 2.42–2.49 (1 H, d, *J* 18.5 Hz, H_{6s}), 2.28–2.40 (2 H, complex m, H_{3s}, H_4), 1.87–2.05 (4 H, complex m $H_{7r,s}H_{8r,s}$), and 0.21 (9 H, s, $Si(CH)_3$). Pure (**4a**) was identical to (**17**) except for the signal at δ 0.21 (9 H) which replaced δ 3.41 (3 H) *m/z* 273 (M^+, ^{37}Cl, 1%), 271 (M^+, ^{35}Cl, 3), 258 (15), 256 (41), 146 (34), 93 (72) and 73 (100); (Found: C, 53.4; H, 6.8; N, 5.3. $C_{12}H_{18}ClNO_2Si$ requires C, 53.1; H, 6.6; N, 5.2%).

(1R*, 2R* *and* 1R*, 2S*) *5-Oxo-1-trimethylsilyloxybicyclo*[2.2.2]*octane-2-carbonitrile* (**4c, d**).—Diene (**3a**) (24.2 g, 0.094 mol) and acrylonitrile (60 ml) were stirred together at room temperature for 28 d. The acrylonitrile was evaporated under reduced pressure and the residue was dissolved in methanol cooled to 0 °C. The solution was cooled to 0 °C and potassium carbonate (3.0 g) was added to it. Stirring the mixture at 0 °C for 30 min gave a green mixture, which after filtration gave a yellow solution. Evaporation of this solution gave a yellow solid which was recrystallised from dichloromethane–pentane to give the *carbonitriles* (**4c, d**) (9.8 g 44%) as pale yellow prisms, m.p. 60–65 °C; $\nu_{max}(CHCl_3)$ 2 945s, 2 850m, 2 240m, 1 730s, 1 600m, 1 370m, 1 325m, 1 145s, and 845s cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 2.8–3.0 (2 H, m, *H*CCN and O=CC*H*H), 1.8–2.6 (8 H, m) and 0.18 (9 H, s, OSi $(CH_3)_3$); *m/z* 237 (M^+, 9%), 222 (100), 195 (11), 169 (97), 156 (49), and 83 (78); (Found: C, 60.8; H, 7.8; N; 6.2. $C_{12}H_{19}NO_2$ requires C, 60.72; H, 8.01; N, 5.9%).

4-(2'-Nitroethyl)cyclohexane-1,3-dione (**5**).—The diene (**3a**) (1.50 g, 5.9 mmol) was dissolved in toluene (10 ml) and the solution was cooled to −78 °C. A solution of nitroethylene in benzene (3.2 M 2.0 ml) was added to the cooled solution which was stirred at solid CO_2–acetone temperature for 3 h and was then allowed to warm to room temperature overnight. Water (5 ml) was added to the pale-yellow solution and the mixture was stirred vigorously for 30 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 25 ml). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to give an oily residue. This was purified by flash column chromatography on silica (75 g) with ethyl acetate as eluant to give the *dione* (**5**) (0.88 g, 81%) as an oil, $\nu_{max}(CHCl_3)$ 1 720s, 1 560s, and 1 375s cm^{-1}; $\delta_H([^2H_6]DMSO$, 250 MHz), 4.37–4.43 (2 H, t, *J* 7.3 Hz, CH_2NO_2), 3.33 (2 H, s, $COCH_2CO$), 2.69–2.74 (2 H, t, *J* 6.7 Hz, $COCH$), 2.3–2.4 (1 H, m, H_4), 2.36–2.42 (2 H, t, *J* 7.3 Hz, $CH_2CH_2NO_2$), and 1.84–2.00 (2 H, quintet, *J* 6.7 Hz, 2 × H_5); *m/z* 185 (M^+, 27), 139 (15), 138 (18), and 77 (100).

5-Methyl-3-trimethylsilyloxycyclohex-2-en-1-one (**2b**).—5-Methylcyclohexane-1,3-dione (**1b**) (12.6 g, 0.10 mol), prepared from ethyl acetoacetate and ethyl crotonate,[14] was dissolved in hexamethyldisilazane (80 ml) with imidazole (0.40 g) and the solution was heated under reflux for 2 h. The solvent was distilled, first at atmospheric pressure, then at the water-pump with the apparatus protected by a solid CO_2 trap. The residue was distilled to give the *enone* (**2b**) (18.8 g, 95%), b.p. 96–98 °C/1.0 mmHg as an oil. $\nu_{max}(CHCl_3)$ 1 640s, 1 600s, and 1 200s cm^{-1}; $\delta_H(CDCl_3$, 80 MHz) 5.43 (1 H, s, CH=CO), 1.9–2.5 (5 H, m, H_2CHCH_2) and 1.05 (3 H, d, *J* 6 Hz, $CHCH_3$).

5-Methyl-1,3-bis(trimethylsilyloxy)cyclohexa-1,3-diene (**3b**). —*Method 1*. Di-isopropylamine (0.71 g) was added to dry THF (10 ml) and the solution was cooled to 0 °C. Butyl-lithium (1.55M in hexane; 3.25 ml) was added to the solution, which was then cooled to −78 °C. Enone (**2b**) (1.0 g, 5.1 mmol) in dry THF (5 ml) was added dropwise to this solution which was stirred for 30

min after addition was complete. Trimethylsilyl chloride (1.25 g) was added and the solution was allowed to warm to room temperature. The solvent was removed by distillation and the residue was purified by Kugelrohr distillation to give the diene (**3b**) (1.19 g, 87%) as an oil, b.p. 60–62 °C/1 mmHg, (lit.,[2] 92 °C/5 mmHg); ν_{max}($CHCl_3$) 2 950s, 1 645s, 1 600s, 1 370m, 1 200s, 1 145s, 855s, and 700s cm^{-1}; δ_H($CDCl_3$, 90 MHz) 4.96 (1 H, d, *J* 2 Hz), 4.51–4.58 (1 H, dd, *J* 5, 2 Hz), 2.5–2.7 (1 H, complex m, C*H*CH_3), 1.9–2.3 (2 H, complex m, CH_2CH), 0.98–1.05 (3 H, d, *J* 6 Hz, CHCH_3), 0.24 (9 H, s, Si(CH_3)$_3$), and 0.19 (9 H, s, Si(CH_3)$_3$).

Method 2. Hexamethyldisilazane (1.08 ml) was added to dry THF (10 ml) and the solution was cooled to 0 °C. Butyl-lithium (1.55M in hexane; 3.25 ml) was added to the solution, which was stirred at 0 °C for 30 min and was then cooled to −78 °C. Enone (**2b**) (1.0 g, 5.1 mmol) in dry THF (5 ml) was added dropwise to the solution, which was then stirred at −78 °C for 30 min. Trimethylsilylchloride (1.25 g) was added and the solution was allowed to warm to room temperature and then filtered. The solvent was distilled and the residue was purified by bulb-to-bulb distillation to give the diene (**3b**) (1.35 g, 99%) b.p. 77–79 °C/3 mmHg identical to that prepared before.

Method 3. Dione (**1b**) (0.62 g, 4.9 mmol) was dissolved in dry ether (10 ml) with triethylamine (1.0.3 g) and the solution was cooled to 0 °C. Trimethylsilyl triflate (2.2 g) in dry ether (2 ml) was added dropwise to the solution, which was then stirred at 0 °C for 15 min. The lower layer was removed by pipette and the solvent was distilled from the top layer. The residue was purified by bulb-to-bulb distillation to give the diene (**3b**) (1.25 g, 95%) as an oil, b.p. 62–64 °C/1.1 mmHg, identical to that prepared before.

(1R*, 2R*, 8S*)-, (1R*, 2S*, 8S*)-, (1R*, 2R*, 8R*)-, *and* (1R*, 2S*, 8R*)-2-*Chloro*-8-*methyl*-5-*oxo*-1-*trimethylsilyloxybicyclo*-[2.2.2]*octane*-2-*carbonitrile* (**4e–h**).—The diene (**3b**) (17.7 g, 0.066 mol), 2-chloroacrylonitrile (19 ml) and dichloromethane (20 ml) were stirred together at room temperature for 7 days. The solution was then evaporated under reduced pressure and the resulting oily residue was dissolved in ice-cooled methanol (200 ml). Powdered, anhydrous potassium carbonate (20 g) was added to the cooled solution, which was stirred at 0 °C for 30 min and was then filtered to remove the solid residues. These were washed with ethyl acetate (2 × 20 ml) and the washings and the filtrate were combined and washed with saturated aqueous sodium hydrogen carbonate (50 ml) and brine (50 ml), dried (Na_2SO_4), filtered and evaporated under reduced pressure to give a pale, yellow oil. This was purified by flash column chromatography on silica gel (500 g) with 30% ethyl acetate–hexane as eluant to give the *ketones* (**4e–h**) (14.8 g, 80%) as a powdery, white solid, m.p. 39.5–41 °C. The ratio of the ketones (**4e**), (**4f**), (**4g**) and (**4h**) was 10:7:1.2:1 as determined by integration of the signals due to the methyl group in the proton NMR and as confirmed by gas chromatography. ν_{max}($CHCl_3$) 1 735s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 2.1–3.0 {7 H, m, $H_{3r,s}$, H_4, $H_{6r,s}$, H_{7r} [of (**4g, h**)], H_8}, 1.47–1.56 (dd, *J* 14, 7.7 Hz) and 1.19–1.27 {dd, *J* 13.2, 6.8 Hz, H_{7s} [of (**4e, f**)]}, 1.01 (**4e**), 0.98 (**4f**), 1.18 (**4g**), 1.15 (**4h**) (3 H all d, *J* 6.7 Hz, Me), and 0.21 (9 H, s, Me_3Si); *m*/*z* 270 (M^+ − CH_3, 30%), 236 (11), 192 (20), 183 (17), and 73 (100); (Found: C, 54.5; H, 6.7; N, 4.7. $C_{13}H_{20}ClNO_2Si$ requires C, 54.6; H, 7.1; N, 4.9%).

General Procedure for Lewic-acid Mediated Cycloadditions.—The diene (**3b**) (0.100 g, 0.35 mmol) was dissolved in the solvent (1 ml) and the solution was cooled to −78 °C. The Lewis acid (1 molar equiv.) was added to the solution, followed by 2-chloroacrylonitrile (0.10 ml). The solution was stirred at −78 °C for 20 h and then water (1 ml) was added. The mixture was allowed to warm to room temperature and then dichloromethane (10 ml) and 3M hydrochloric acid (10 ml) were added to it. The aqueous layer was extracted with dichloromethane (3 × 10 ml) and the combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (5 g) with 30% ethyl acetate–hexane as eluant. In this way a mixture of the ketones (**4e–h**) was obtained. The diastereoisomer ratio was determined by NMR and GC analysis.

(1R*, 2R*) *and* (1R*, 2S*)-2-*Chloro*-1-*hydroxy*-5-*oxobicyclo*-[2.2.2]*octane*-2-*carbonitrile* (**8a, b**).—The mixture of adducts (**4a, b**) (155 mg, 0.57 mmol) was dissolved in THF (3 ml) and the solution was cooled to 0 °C. Tetrabutylammonium fluoride in THF (0.65 ml of a 1M solution) was added dropwise to this solution, which was then stirred at 0 °C for 4 h. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (10 g) with 50% ethyl acetate–hexane as eluant. The first eluted compounds were the mixture of *keto alcohols* (**8a, b**) which were recrystallised from dichloromethane–pentane to give tiny prisms, m.p. 87–88 °C (82 mg, 74%). The keto alcohols could also be prepared from the ethers (**4a, b**) by reaction with potassium carbonate in methanol at room temperature over 5 h. In this way a 95% yield of (**8a, b**) could be obtained; ν_{max}($CHCl_3$) 3 600s, 3 300–3 500br, 2 950s, 2 240w, 1 730s, and 1 600m cm^{-1}; δ_H($CDCl_3$, 250 MHz) 2.9–3.0 (1 H, m, H_{6r}), 2.4–2.8 (4 H, m, H_{6s}, $H_{3r,s}$, H_4), 1.9–2.3 (4 H, m, $H_{7r,s}$, $H_{8r,s}$), 1.6 (1 H, br s, OH); *m*/*z* 199 (M^+, 15%), 164 (11), 163 (49), 136 (25), and 112 (100); (Found: C, 54.4; H, 5.1; N, 7.0. $C_9H_{10}ClNO_2$ requires, C, 54.1; H, 5.0; N, 7.0%).

(6R*, 8R*)-3-*Oxo*-9-*oxabicyclo*[4.3.0]*non*-1(2)-*en*-8-*carbonitrile* (**9a**) *and* (6R*, 8S*)-3-*Oxo*-9-*oxabicyclo*[4.3.0]*non*-1(2)-*ene*-8-*carbonitrile* (**9b**).—Tetrabutylammonium fluoride (2 ml of a 1M solution in THF) was stirred over 4 Å molecular sieves for 24 h. The solution was then cooled to 0 °C and the bicyclic ketone adducts (**4a, b**) (343 mg, 1.26 mmol) in THF (4 ml) was added to it over 40 min. The resulting brown mixture was stirred at room temp. for 2 days and was then filtered to remove the solid. The solid residues were washed with ether (5 ml) and the liquid layer and washings were combined and washed with water (5 ml). The aqueous layer was extracted with ether (3 × 5 ml) and the organic layers were all combined. Charcoal (0.5 g) was added to the combined layers and the suspension was stirred for 30 min and was then filtered through a Celite plug. This was washed with ether (10 ml) and the combined organic extracts were dried (Na_2SO_4), filtered and evaporated to give an oil. This was purified by flash column chromatography on silica gel (50 g) with 75% ethyl acetate–hexane as eluant. This gave the two enones (**9a**) (120 mg, 58%) and (**9b**) (61 mg, 30%) as oils which crystallised on standing to give the *enone* (**9a**) as prisms m.p. 63.5–65 °C and the *enone* (**9b**) as a microcrystalline solid m.p. 69–70 °C.

Enone (**9a**); ν_{max}($CHCl_3$) 2 950m, 2 250w, 1 650s, 1 600m, 1 370s, 1 150s, and 960s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 5.55 (1 H, s, H_2), 5.02–5.09 (1 H, dd, *J* 11.1, 5.7 Hz, H_8), 2.95–3.10 (1 H, m, H_6), 2.75–2.87 (1 H, dt, *J* 11.9, 6.2, 5.7 Hz, H_7), 2.04–2.19 (1 H, *q*, *J* 12 Hz, H_7), 2.46–2.55 (1 H, m, H_4), 2.21–2.38 (2 H, m, $H_{5r,s}$), and 1.68–1.86 (1 H, m, H_4); δ_C($CDCl_3$, 62.9 MHz), 197.9 (C-3), 178.4 (C-1), 115.8 (C-9), 102.6 (C-3), 69.2 (C-8), 39.1, 35.8, 35.7, 27.1; *m*/*z* 163 (M^+, 37%), 135 (100) and 71 (73); (Found: C, 66.4; H, 5.6; N, 8.8. $C_9H_9NO_2$ requires C, 66.2; H, 5.6; N, 8.9%).

Enone (**9b**); ν_{max}($CHCl_3$) 2 950m, 1 650s, 1 600m, 1 370m, 1 155s, and 980s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 5.52 (1 H, d, *J* 1.1 Hz, H_2), 5.23–5.29 (1 H, d, *J* 8.4 Hz, H_8), 3.32–3.41 (1 H, ddddd, *J* 12.6, 7.6, 6, 5, 1.1 Hz, H_6), 2.63–2.71 (1 H, dd, *J* 12.8, 7.5 Hz, H_{7r}), 2.28–2.56 (2 H, m, H_4 and H_{5r}, H_{5s}), 2.07–2.21 (1 H, dt, *J* 8.4, 12.6 Hz, H_{7s}), and 1.58–1.80 (1 H, m, H_4); δ_C($CDCl_3$, 62.89 MHz), 198.0 (C-3), 178.8 (C-1), 116.1 (C-9), 102.7 (C-2), 69.5 (C-

8), 38.2, 35.8, 35.4, and 27.0; *m/z* 163 (M^+, 17%), 135 (68), and 69 (100); (Found: M^+, 163.0621. $C_9H_9NO_2$ requires *M*, 163.0634).

(1R*, 2R*, 5R*)-, (1R*, 2R*, 5S*)-, (1R*, 2S*, 5R*)-, *and* (1S*, 2R*, 5R*)-2-*Chloro*-1,5-*dihydroxybicyclo*[2.2.2]*octane*-2-*carbonitrile* (**14a**).

The ketones (**4a, b**) (1.00 g, 5 mmol) were dissolved in methanol (15 ml) and the solution was cooled to 0 °C. Sodium borohydride (0.25 g) was added to the solution, which was stirred at 20 °C for 1 h. A further portion of sodium borohydride (0.25 g) was added to the solution, and stirring was continued for 1 h at 20 °C.

The methanolic solution was acidified with 3M hydrochloric acid, and the organic solvent was evaporated under reduced pressure. The residue was partitioned between water (10 ml) and ethyl acetate (10 ml). The aqueous phase was extracted with ethyl acetate (4 × 10 ml) and the combined organic phases were dried ($MgSO_4$). The solvent was filtered and then was evaporated under reduced pressure to yield a white solid. This was purified by flash column chromatography on silica gel (25 g) with 75% ethyl acetate–hexane as eluant to yield the *diol* (**14a**) (0.575 g, 78%) as a mixture of diastereoisomers. A sample recrystallised from dichloromethane–pentane started to decompose at 80 °C, presumably by the usual [2.2.2] to [3.2.1] rearrangement pathway. Crystallisation of the product as another form then took place; $\nu_{max}(CHCl_3)$ 3 600s, 3 200–3 500br, 2 950s, and 1 600m cm^{-1}; $\delta_H(CDCl_3$, 250 MHz), 4.13–4.18 (1 H, m, C*H*OH), 1.5–2.9 (11 H, m, remaining protons); *m/z* (CI) 219 [(M + NH_4^+, 77%], 185 (100) and 169 (26); (Found: C, 53.8; H, 6.0; N, 7.0. $C_9H_{12}ClO_2N$ requires C, 53.6; H, 6.0; N, 7.0%).

(1R*, 2R*, 5R*)-, (1R*, 2R*, 5S*)-, (1R*, 2S*, 5R*)-, *and* (1S*, 2R*, 5R*)-2-*Chloro*-5-*hydroxy*-1-*trimethylsilyloxybicyclo*-[2.2.2]*octane*-2-*carbonitrile* (**14b**).—The ketones (**4a, b**) (0.10 g, 0.5 mmol) were dissolved in methanol (1.0 ml) and THF (0.2 ml) and the solution was cooled to 0 °C. Sodium borohydride (26 mg) was added to the cooled solution, which was stirred at 0 °C for 3 h. Saturated ammonium chloride (2.5 ml) was then added to the clear solution, and the organic solvents were removed under reduced pressure. The aqueous phase was extracted with ethyl acetate (3 × 10 ml) and the combined organic extracts were washed with brine (5 ml), dried (Na_2SO_4) and evaporated under reduced pressure to give a pasty solid. This was purified by preparative TLC on silica to give the alcohol (**14b**) (0.056 g, 56%) as a mixture of diastereoisomers; $\nu_{max}(CHCl_3)$ 3 200–3 600s, 2 900s, 1 600s, 1 160s, and 850s cm^{-1}; $\delta_H(CDCl_3$, 90 MHz) 4.05–4.25 (1 H, m, C*H*OH), 1.2–3.0 (11 H, m, bicyclic protons), and 0.2 (9 H, s, $Si(CH_3)_3$); *m/z* 273 (M^+, 8%), 258 (32), 240 (4) and 87 (100).

(5R*, 6S*, 8R*)- *and* (5R*, 6S*, 8S*)-3-*Oxo*-9-*oxabicyclo*-[4.3.0]*non*-1(2)-*en*-8-*carbonitrile* (**9c**) *and* (**9d**).—Tetrabutylammonium fluoride (4 ml; 1M solution in THF) was added to dry THF (20 ml) and the solution was stirred over 4 Å sieves for 24 h. The ketones (**4e, f**) (1.14 g, 4 mmol) were dissolved in dry THF (20 ml) and this solution was added dropwise to the dried solution of tetrabutylammonium fluoride. The solution was stirred for 5 days and was then filtered. The filtrate was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica (50 g) with 75% ethyl acetate for hexane as eluant. The first eluted compound was the deprotected ether (0.036 g, 4%) followed by the enone (**9c**) (0.163, 23%), as rhombuses, m.p. 148.5–149.5 °C, and the enone (**9d**) (0.150, 21%) as prisms, m.p. 130–132 °C.

For enone (**9c**); $\nu_{max}(CHCl_3)$ 2 920s, 1 640s, 1 370s, and 1 150s cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 5.55–5.56 (1 H, d, *J* 1.4 Hz, H_2), 5.26–5.29 (1 H, d, *J* 8.4 Hz, H_8), 2.88–3.01 (1 H, ddt, *J* 7.4, 1.4, 12.7 Hz, H_6), 2.67–2.75 (1 H, dd, *J* 12.7, 7.4 Hz, H_{7r}), 2.44–2.51 (1 H, dd, *J* 16.5, 3.6 Hz, H_{4r}), 2.18–2.07 (1 H, dd, *J* 16.5, 14.2 Hz, H_{4s}), 2.17–2.03 (1 H, dt, *J* 8.4, 12.7 Hz, H_{7s}), 1.90–2.05 (1 H, ddd, *J* 14.2, 12.7, 3.6 Hz, H_5), and 1.15–1.18 (3 H, d, *J* 6.3 Hz, CH_3); *m/z* 177 (M^+, 21%), 135 (100), and 119 (13).

For *enone* (**9d**); $\nu_{max}(CHCl_3)$ 2 950s, 1 640s, 1 370s, 1 345s, and 1 160s cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 5.55–5.56 (1 H, d, *J* 1.1 Hz, H_2), 5.00–5.07 (1 H, dd, *J* 11.1, 5.7 Hz, H_8), 2.84–2.89 (1 H, m, H_7), 2.70–2.82 (1 H, m, H_6), 2.40–2.54 (1 H, m, H_4), 1.96–2.16 (3 H, m, H_4, H_7, and H_5), and 1.12–1.15 (3 H, d, *J* 6.1 Hz, CH_3); *m/z* 177 (M^+, 22%), 135 (69), and 69 (100); (Found: C, 67.5; H, 6.4; N, 8.1. $C_{10}H_{11}NO_2$ requires C, 67.8; H, 6.6; N, 7.9%).

(1R*, 6R*, 8R*)-9-*Oxabicyclo*[4.3.0]*non*-2(3)-*en*-8-*carbonitrile* (**15a**).—The enone (**9a**) (26 mg) was dissolved in THF (4 ml) and the solution was cooled to −78 °C. Borane–THF complex (0.58 ml; 1M solution in THF) was added to this solution at −78 °C, and the solution was then allowed to warm slowly to room temperature. Acetic acid (0.3 ml) was added to the solution, which was stirred at room temperature for 2 h before being neutralised by addition of sodium hydrogen carbonate. The solution was then evaporated to dryness and the residue was partitioned between water (1 ml) and dichloromethane (2 ml). The aqueous layer was extracted with dichloromethane (3 × 2 ml) and the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (2 ml) with 30% ethyl acetate–hexane as eluant. The *cyclohexene* (**15a**) (17 mg, 72%) was the first eluted compound, isolated as an oil. In addition the starting material (3 mg, 12%) was recovered; $\nu_{max}(CHCl_3)$ 2 950s, 2 850s, 1 600m, and 1 460m cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 5.75–5.79 (1 H, br d, *J* 10.1 Hz), and 5.64–5.69 (1 H, dd, *J* 10.1, 1.1 Hz, H_2 and H_3), 4.54–4.60 (1 H, t, *J* 6.1 Hz, H_8), 4.21–4.26 (1 H, m, H_1), and 1.3–2.3 (7 H, m); *m/z* 149 (M^+, 1%), 131 (11), 121 (15), and 57 (100); (Found: M^+, 149.0845. $C_9H_{11}NO$ requires *M*, 149.0840).

(1R*, 6R*, 8S*)-9-*Oxabicyclo*[4.3.0]*non*-2(3)-*en*-8-*carbonitrile* (**15b**).—The enone (**9b**) (48 mg) was dissolved in THF (4 ml) and the solution was cooled to −78 °C. Borane–THF complex (0.29 ml; 1M solution in THF) was added dropwise to the solution, which was allowed to warm to room temperature overnight. The solution was then quenched with acetic acid (0.15 ml), and was stirred at room temperature for 2 h before being neutralised by addition of sodium hydrogen carbonate. The mixture was evaporated to dryness and the residue was partitioned with water (1 ml) and dichloromethane (2 ml). The aqueous layer was extracted with dichloromethane (3 × 2 ml) and the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (2 ml) with 30% ethyl acetate–hexane as eluant to give the *cyclohexene* (**15b**) (13 mg, 30%) and recovered starting material (19 mg, 40%); $\nu_{max}(CHCl_3)$ 2 950s, 2 850s, 1 600w, and 1 100m cm^{-1}; $\delta_H(CDCl_3$, 250 MHz) 5.95–6.02 (1 H, br d, *J* 10.1 Hz) and 5.76–5.83 (1 H, br d, *J* 10.1 Hz, H_2 and H_3), 4.60–4.66 (1 H, dd, *J* 8.7, 5.6 Hz, H_8), 4.30–4.33 (1 H, m, H_1), 2.3–2.5 (2 H, m, 2 × H_7), 1.9–2.1 (3 H, m, 2 × H_4 and H_6), and 1.7–1.8 (2 H, m, H_5); *m/z* 149 (M^+, 2%), 121 (17), 96 (16), and 56 (100); (Found: M^+, 149.0837. $C_9H_{11}NO$ requires, *M*, 149.0840).

1-*Methoxy*-3-*trimethylsilyloxycyclohexa*-1,3-*diene* (**16a**; *R* = H).—3-Methoxycyclohex-2-enone (1.26 g, 10 mmol) was added dropwise to a solution of lithium di-isopropylamide [made from di-isopropylamine (1.40 ml) and butyl-lithium (6.45 ml; 1.55M solution in hexane)] in THF (10 ml) at −78 °C. The resulting yellow solution was stirred at −78 °C for 30 min and was then quenched with trimethylsilyl chloride (1.52 ml, 12 mmol). The

solution was allowed to warm to room temperature and was then filtered and the low boiling point liquids were distilled off at atmospheric pressure. Distillation of the residue gave the diene (**16a**; R=H) (1.59 g, 80%) b.p. 90–91 °C/4 mmHg; ν_{max}($CHCl_3$) 2 960s, 2 840m, 1 655s, 1 610s, 1 380s, 1 260s, 1 150s, and 860s cm^{-1}; δ_H($CDCl_3$, 90 MHz) 4.65 (1 H, d, *J* 1 Hz), COMe=C*H*), 4.5 (dt, *J* 1, 7 Hz, =C*H*), 3.55 (3 H, s, OCH_3), 2.25 (4 H, m, CH_2CH_2), 0.28 (9 H, s, $OSiMe_3$); *m/z* 197 (M^+ − H, 2.5%), 91 (76), 86 (95), 75 (87), and 73 (100).

(1R*, 2S*)-2-*Chloro*-1-*methoxy*-5-*oxobicyclo*[2.2.2]*octane*-2-*carbonitrile* (**17**), 2-*Methoxy*-6-*oxobicyclo*[3.2.1]*oct*-2-*ene*-1-*carbonitrile* (**18**) *and* 2-*Methoxy*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-3-*carbonitrile* (**19**).—The diene (**16a**; R=H) (100 g, 5.1 mmol) was dissolved in 2-chloroacrylonitrile (5 ml) and the mixture was heated at 70 °C for 1 h. The mixture was poured onto methanol (10 ml) with potassium carbonate (0.5 g) and the resultant slurry was stirred at room temperature overnight. The solvent was then removed under reduced pressure. The residue was partitioned between water (25 ml) and ethyl acetate (25 ml) and the aqueous layer was extracted with ethyl acetate (3 × 25 ml). The combined organic phases were washed with saturated aqueous sodium hydrogen carbonate (25 ml), and brine (25 ml), dried (Na_2SO_4) and evaporated under reduced pressure to yield a solid residue. This was purified by flash column chromatography on silica gel (100 g) with 30% ethyl acetate–hexane as eluant to give, in order of increasing polarity; the ketone (**17**) (0.41 g, 38%) as prisms m.p. 108–108.5 °C; the enol ether (**18**) (0.13 g, 4%) as prisms m.p. 88–89 °C and the ketone (**19**) (0.16 g, 15%) as prisms m.p. 113–113.5 °C.

For *ketone* (**17**); ν_{max}($CHCl_3$) 2 950s, 1 730s, 1 600m, and 1 200s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 3.41 (3 H, s, OCH_3), 2.86–2.94 (1 H, dd, *J* 15.6, 2.8 Hz, H_{3s}), 2.81–2.91 (1 H, dt, *J* 18.6, 2.7 Hz, H_{6r}), 2.55–2.62 (1 H, d, *J* 18.6 Hz, H_{6s}), 2.50–2.59 (1 H, dt, *J* 15.6, 2.7 Hz, H_{3r}), 2.40–2.44 (1 H, quintet, *J* 2.7 Hz, H_4), 2.14–2.22 (2 H, m, H_7 or 2 × H_8) and 1.94–2.02 (2 H, m, H_7 or 2 × H_8); δ_C($CDCl_3$, 62.9 MHz) 207.1 (C-5), 118.7 (CN), 78.1 (OCH_3), 60.6 (C-1), 51.3 (C-2), 43.1, 42.0, 41.4 (C-3, C-4, and C-6), 24.8, 21.1 (C-7 and C-8); *m/z* 213 (M^+, 5%), 178 (2), 126 (68), and 98 (100); (Found: C, 56.1; H, 5.7; N, 6.6. M^+, 213.0577. $C_{10}H_{12}ClNO_2$ requires, C, 56.2; H, 5.7; N, 6.6%. M, 213.0556).

For *enol ether* (**18**); ν_{max}($CHCl_3$) 2 950s, 2 250m, 1 750s, 1 660s, 1 600w, 1 460s, 1 360s, 1 200s, and 1 115s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 4.43–4.45 (1 H, dd, *J* 4.5, 2.6 Hz, H_3), 3.59 (3 H, s, OCH_3), 2.78–2.87 (1 H, dt, *J* 17.3, 1.1 Hz, H_{7s}), 2.67–2.73 (1 H, d, *J* 17.3 Hz, H_{7r}), 2.70–2.75 (1 H, m, H_5), 2.44–2.52 (2 H, m, H_{8r}, H_{8s}), 2.41–2.49 (1 H, ddd, *J* 16.7, 5.1, 2.6 Hz, H_8), and 2.17–2.27 (1 H, ddd, *J* 16.7, 4.5, 2.1 Hz, H_8); δ_C($CDCl_3$, 62.9 MHz) 213.7 (s, C-6), 154.5 (s, C-2), 119.0 (s, CN), 89.6 (d, C-3), 55.4 (q, OCH_3), 52.1 (t, C-4 or C-7), 44.4 (d, C-5), 39.3 (s, C-1), 38.1 (t, C-4 or C-7), and 27.9 (t, C-8); *m/z* 177 (M^+, 94%), 162 (8), 149 (9), 135 (100), and 75 (48); (Found: C, 67.6; H, 6.3; N, 7.8; M^+, 117.0789. $C_{10}H_{11}NO_2$ requires C, 67.8; H, 6.3; N, 7.9%. *M*, 177.0789).

For ketone (**19**); ν_{max}($CHCl_3$) 2 930m, 2 220m, 1 735s, 1 325m, and 1 120s cm^{-1}; δ_H($CDCl_3$, 250 MHz) 3.48 (3 H, s, OCH_3), 2.53 (1 H, d, *J* 1.5 Hz), 2.40–2.51 (1 H, ddd, *J* 12.0, 5.8, 2.2 Hz), 2.35–2.42 (1 H, m), 2.13–2.18 (1 H, d, *J* 12.0 Hz), and 1.62–1.88 (2 H, m); δ_C($CDCl_3$, 62.9 MHz) 205.6, 117.0, 76.5, 73.2, 55.5, 40.6, 40.2, 30.4, 26.4, 23.6, and 18.5; *m/z* 177 (M^+, 2%), 149 (64), 126 (100), and 121 (25); (Found: C, 67.1; H, 6.2; N, 7.7. $C_{10}H_{11}NO_2$ requires C, 67.8; H, 6.3; N, 8.0%).

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References

1 R. H. Schlessinger, in 'Organic Synthesis, Today and Tomorrow,' Proceedings of the 3rd IUPAC Symposium on Organic Synthesis, 1980, ed. B. M. Trost and C. R. Hutchinson, Pergamon, Oxford, 1981, p. 251; K. B. White and W. Reusch, *Tetrahedron*, 1978, **34**, 2439; H. Nagaoka, K. Kobayashi, T. Okamura, and Y. Yamada, *Tetrahedron Lett.*, 1987, **28**, 6641.
2 T. Ibuka, Y. Muri, T. Aoyama, and Y. Inubushi, *Chem. Pharm. Bull.*, 1978, **26**, 456.
3 K. Krageloh and G. Simchen, *Synthesis*, 1981, 30.
4 S. Torkelson and C. Ainsworth, *Synthesis*, 1976, 722.
5 S. Torkelson and C. Ainsworth, *Synthesis*, 1977, 431.
6 D. T. Hurst and A. G. McInnes, *Can. J. Chem.*, 1965, **43**, 2004.
7 W. E. Noland, *Org. Synth.*, 1961, **41**, 57; S. Kambe and H. Yasuda, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 1444.
8 J. E. McMurry and J. H. Musser, *Org. Synth.*, 1977, **56**, 65.
9 K. Maruoka, T. Itoh, T. Shirosaka, and H. Yamamoto, *J. Am. Chem. Soc.*, 1988, **110**, 310; K. Maruoka and H. Yamamoto, *Tetrahedron*, 1988, **44**, 5001; W. G. Earley, E. J. Jacobsen, G. P. Meier, T. Oh, and L. E. Overman, *Tetrahedron Lett.*, 1988, **29**, 3781.
10 S. A. Monti, S.-C. Chen, Y.-L. Yang, and O. P. Bourgeois, *J. Org. Chem.*, 1978, **43**, 4062; D. A. Evans, W. L. Scott and L. K. Truesdale, *Tetrahedron Lett.*, 1972, **13**, 121; N. C. Madge and A. B. Holmes, *J. Chem. Soc., Chem. Commun.*, 1980, 956; *Tetrahedron*, 1989, **45**, 789.
11 E. Vieira and P. Vogel, *Helv. Chim. Acta*, 1982, **65**, 1700.
12 E. J. Cory and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190.
13 E. J. Cory and A. W. Gross, *Tetrahedron Lett.*, 1984, **25**, 495; E. J. Corey and N. W. Boaz, *ibid*, 1985, **26**, 6019; A. Alexakis, J. Berlan, and Y. Besace, *ibid*, 1986, **27**, 1047.
14 A. W. Crossley and N. Renouf, *J. Chem. Soc.*, 1915, 602.

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