Nitrobicyclo[2.2.1]heptanes. Part 7.[1] The Synthesis of Eight Isomeric Nitrobicyclo[2.2.1]heptan-2-ols and of Four Isomeric Nitrobicyclo[2.2.1]-heptan-2-ones

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Diels–Alder reaction of 2-nitropropene and cyclopentadiene yields a separable mixture (85:15) of 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]heptene (**1a**) and the *endo*-methyl-*exo*-nitro epimer (**1b**). Hydroboration–oxidation of each in turn gives separable mixtures of 6- and 5-*endo*-nitrobicyclo-[2.2.1]heptan-2-*exo*-ols (**2a**)/(**3a**) and the *exo*-nitro analogues (**2b**)/(**3b**) respectively, with the 6-nitro isomers (**2**) predominating by *ca.* 3:1 in each case. Oxidation of the four alcohols with ruthenium tetraoxide gives the four ketones (**4a**), (**4b**), (**5a**), and (**5b**), from which the corresponding *endo*-alcohols (**7**) and (**8**) are prepared by reduction with sodium borohydride or with K-selectride. ^{1}H and ^{13}C N.m.r. data are tabulated for all compounds, and some trends in chemical shifts are described.

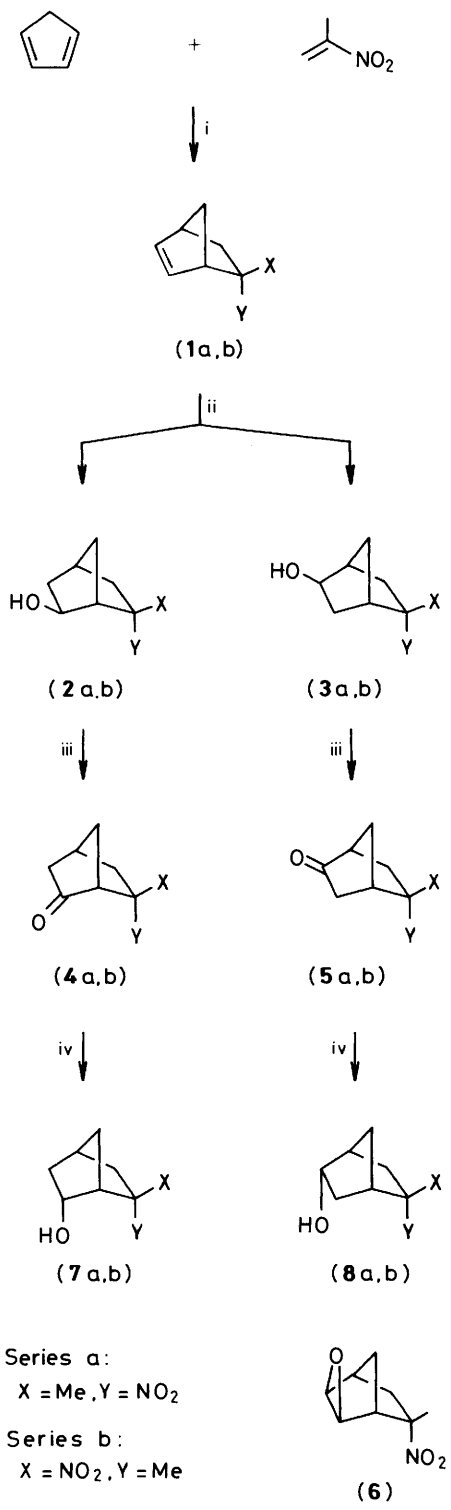
Our previously published reports of crystallographically discernible intra-[2] and inter-molecular[3] hydroxy-to-nitro hydrogen bonds in a number of nitrobicyclo[2.2.1]heptanols (nitronorbornanols) have spearheaded a search in these laboratories for other examples of this somewhat uncommon interaction. The rigid skeleton of the readily accessible norbornyl system lends itself to the regio- and stereo-chemically unambiguous placing of substituents, making it a convenient clotheshorse on which to hang functional groups potentially capable of interaction. Our aim is to look for correlations between the solid-state packing modes of appropriate compounds and the spatial disposition of the interacting functional groups, and to relate both to the types of hydrogen bond, if any, that may be present. Our studies have up to now depended on the chance preparation of suitably substituted norbornanes. In this paper we report the systematic synthesis of a group of isomeric nitronorbornanols, the structures of several of which are now under investigation.

The Diels–Alder cycloaddition of cyclopentadiene and nitroalkenes is a well-precedented and generally favourable reaction that gives adducts in which the nitro group is predominantly *endo*.[4] In principle, hydroxylation of the C=C bond of such adducts should give norbornanes in which the functional groups of interest have a 2,5 or 2,6 relationship to each other. This is effectively the strategy on which the present work is based. We wished to avoid loading the system with substituents other than the two under consideration, but past experience[3] has taught us that the nitro group is very easily isomerised from the *endo* to the *exo* position, presumably by way of an *aci*-nitro tautomer. To prevent this stereochemical scrambling, we chose to block epimerisation by placing a methyl group geminal to the nitro group.

The synthetic transformations involved are shown in the Scheme, which begins with a Diels–Alder reaction of 2-nitropropene and cyclopentadiene. This reaction has previously been reported,[5] but without analysis of the stereochemical outcome. We carried out the reaction at room temperature in ether, and found two adducts in the ratio 85:15 (n.m.r., gas chromatography). Partial separation of the adduct mixture was possible with the aid of medium pressure column chromatography on silica gel, and yields of the *endo*-nitro compound (**1a**) (81%), the minor adduct (**1b**) (10.5%), and an unseparated fraction (8%) are typical of the results we obtained reproducibly on multi-gram scales. The assignment of stereochemistry was made with the aid of n.m.r. spectroscopy, since the nitro group deshields the *syn*-vicinal proton on C-6 significantly (see below). In compound (**1a**), the 6-*endo* proton resonates at δ 2.33; its stereochemistry is confirmed by the long-range W-coupling[6] of 3.4 Hz to the 7-H proton *syn* to the double bond. In compound (**1b**), the deshielded 6-*exo* proton (δ 2.84) has a coupling constant (3.9 Hz) typical[6] of an *exo* proton coupled to a bridgehead position (here, to 1-H). The melting points [68—69 °C for (**1a**) and 64—67 °C for (**1b**)] differ from the reported[5] melting point of the adduct (104 °C), though this last value should be treated circumspectly in view of the stereochemical ambiguity in the earlier work.

Preparation of the 2-*exo*-hydroxy isomers of the desired nitronorbornanols was by hydroboration–oxidation on the less hindered face of the Diels–Alder adducts (**1a**) and (**1b**). While excellent *exo*-stereoselectivity has been reported in the hydroboration of norbornene itself with borane–tetrahydrofuran,[7] we had little success with this reagent. The reagent of choice was borane–dimethyl sulphide followed by alkaline peroxide cleavage, according to the procedure established by Lane[8] for norbornene. We found substantial regioselectivity in this reaction: hydroboration and oxidation of the *endo*-nitronorbornene (**1a**) gave 6-*exo*-methyl-6-*endo*-nitrobicyclo[2.2.1]-heptan-2-*exo*-ol (**2a**) and the 5-*endo*-nitro-2-*exo*-hydroxy isomer (**3a**) in consistent yields of *ca.* 53 and 18% respectively. These alcohols were separable by column chromatography. Similarly, hydroboration–oxidation of the *exo*-nitronorbornene (**1b**) gave the 6- and 5-nitro-2-*exo*-alcohols (**2b**) and (**3b**) in yields of 44 and 14% respectively. Although isolated yields were by no means quantitative, we could detect no *endo*-alcohols in the crude product mixtures (t.l.c.). The regioselectivity of hydroboration must simply reflect the transmission of the inductive effects of the nitro group through the sigma framework of the molecule to the double bond. It is known that these effects (possibly tempered by neighbouring group and frangomeric effects) are quite pronounced when electrophilic reagents such as H^+ are added to 5-nitronorbornene itself,[9] and in these examples the electrophile does, in fact, add preferentially to the vinylic carbon atom closest to the nitro group.

Several different methods were tried for the oxidation of the four alcohols described above to the corresponding ketones. Our first choice was a Swern oxidation[10] with dimethyl



Scheme. *Conditions:* i, Ether, r.t.; ii, BH_3·Me_2S/THF; iii, RuO_2(cat.)/$NaIO_4$/MeCN–CCl_4–H_2O; or DMSO/$(COCl)_2$/NEt_3; iv, $NaBH_4$/$EtBH_4$/EtOH; or K-selectride/THF

sulphoxide activated by a suitable electrophile, since this method has been used successfully for the oxidation of bicyclic alcohols. Trial experiments showed that the best activator for our purpose was oxalyl chloride. Oxidation of (**2a**) proceeded very cleanly under standard conditions[11] to give 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]heptan-2-one (**4a**) in 79% yield. Similar oxidation of (**3a**) gave the 5-*endo*-nitro-2-one (**5a**) in 68% yield.

Though the Swern oxidations proved to be very satisfactory, the experimental conditions are rather demanding. We therefore examined oxidations with ruthenium tetraoxide, generated *in situ* by the action of sodium periodate on ruthenium dioxide in a two-phase water–tetrachloromethane mixture. The procedure of Sharpless,[12] in which acetonitrile is used as co-solvent to aid in the chelation of low-valent ruthenium species, was followed. The reaction proved in general to be even more successful than the Swern oxidation, besides being much easier to carry out experimentally. Oxidation of (**2a**) and (**3a**) gave ketones (**4a**) and (**5a**) in 73 and 79% yields respectively. Similarly, oxidation of the *exo*-nitro alcohols (**2b**) and (**3b**) gave the *exo*-nitro ketones (**4b**) and (**5b**) in 88 and 72% yields respectively.

Two other routes to the ketones (**4a**) and (**5a**) were unsuccessful. Direct synthesis from nitronorbornene (**1a**) by hydroboration and oxidation with chromic acid[13] was poor. Although the products were formed in a ratio of 10:7 (n.m.r.), they proved to be very difficult to separate from each other. Removal of inorganic by-products affected the mass balance adversely, and the isolated yield of the mixture was unacceptable (17%). An alternative approach involved attempted rearrangement[14] of the 2,3-*exo*-epoxide (**6**), which was obtained from (**1a**) and *m*-chloroperoxybenzoic acid in 55% yield. The pinacol-like rearrangement of norbornyl epoxides to norbornanones is in general not favoured,[15] so it was not surprising that the epoxide (**6**) was recovered unchanged, or otherwise completely decomposed, after treatment with various Lewis acids. We have previously shown that the nor-methyl analogue of (**6**) rearranges to 1-nitrotricyclo[2.2.1.$0^{2,6}$]heptan-3-ol on treatment with anhydrous magnesium bromide.[16]

The four *endo*-alcohols (**7a**), (**7b**), (**8a**), and (**8b**) were prepared by straightforward reduction of the precursor ketones (**4**) and (**5**) with hydride reagents, hydride delivery being onto the more accessible *exo*-face of the carbonyl group. Our initial reactions were performed with Selectrides,[17] since the steric requirements of these bulky reductants were expected to guarantee a high degree of stereoselectivity. This was indeed observed in the reduction of the ketones (**5a**) and (**6a**), but the isolated yields of the *endo*-alcohols (**7a**) and (**8a**), 66 and 41% respectively, were disappointing. The problem appeared to lie in the hydrolysis of the boron-containing reaction intermediate, which could generally be detected (n.m.r.) in the crude product mixtures even after vigorous hydrolysis attempts with aqueous acid or even peroxide. For the less abundant ketones (**4b**) and (**5b**) of the *exo*-nitro series, we just carried out the reductions with sodium borohydride. Work-up proved to be very easy; we found no substantial re-formation of the *exo*-alcohols and were, in fact, able to isolate 6-*endo*-methyl-6-*exo*-nitrobicyclo[2.2.1]heptan-2-*endo*-ol (**7b**) in 93% yield, and the 5-*exo*-nitro-2-*endo*-hydroxy isomer (**8b**) in 95% yield.

Systematic n.m.r. data, particularly ^{13}C data,[18] for nitro substituted norbornanes are not easy to come by. With access to the complete series of isomers described in this work, we have been able to compile a useful set of comparative ^1H and ^{13}C n.m.r. data (Tables 1—3). Exhaustive decoupling experiments and, where necessary, *J*-resolved spectra were used to assign ^1H signals; while H-C correlated spectra were essential for assigning ^{13}C signals. As was indicated previously, the crucial distinction between signals for *endo* and *exo* protons was invariably made on the basis of long-range W-coupling between 7-H and *endo*-H on the one hand, and sizeable coupling between *exo*-H and bridgehead-H on the other. The former also permits differentiation between *syn* and *anti* protons on C-7.

Rationalisation of the observed chemical shifts in compounds (**1**) to (**8**) is complicated by the interplay of effects between the polar functional groups present, and (especially for δ_C

Table 1. ^{1}H Chemical shifts (δ, $CDCl_3$, p.p.m. from TMS)[a]

	1-H	2n-H	2x-H	3n-H	3x-H	4-H	5n-H	5x-H	6n-H	6x-H	7s-H	7a-H	Me	OH
2-ene, 5x-Me-5n-NO_2 (**1a**)[b]	2.93	6.30[c]		6.00[c]		3.20	—	—	2.33	1.80	1.66	1.66	1.84	—
5n-Me-5x-NO_2 (**1b**)[d]	2.94	6.34[c]		6.13[c]		3.45	—	—	1.36	2.84	1.67	1.56	1.54	—
2x-OH, 6x-Me-6n-NO_2 (**2a**)[b]	2.50	3.69	—	1.75	1.38	2.35	2.39	1.54	—	—	1.80	1.49	1.66	2.05
6n-Me-6x-NO_2 (**2b**)[d]	2.90	4.15	—	1.78	1.35	2.42	1.29	2.74	—	—	1.68	1.44	1.62	2.90
5x-Me-5n-NO_2 (**3a**)[b]	2.24	3.86	—	1.66	1.34	2.57	—	—	2.39	1.60	1.82	1.55	1.66	1.56
5n-Me-5x-NO_2 (**3b**)[d]	2.26	3.80	—	2.02	1.41	2.92	—	—	1.19	2.85	1.75	1.38	1.57	1.78
2n-OH, 6x-Me-6n-NO_2 (**7a**)[b]	2.75	—	4.39	1.13	2.11	2.32	2.76	1.74	—	—	1.48	1.63	1.66	1.53
6n-Me-6x-NO_2 (**7b**)[d]	3.05	—	4.47	1.01	2.11	2.34	1.63	3.00	—	—	1.28	1.40	1.91	2.59
5x-Me-5n-NO_2 (**8a**)[d]	2.42	—	4.26	0.88	2.03	2.53	—	—	3.14	1.57	1.55	1.69	1.71	2.07
5n-Me-5x-NO_2 (**8b**)[d]	2.37	—	4.27	1.29	2.00	2.89	—	—	2.18	2.65	1.44		1.71	2.00
2-one, 6x-Me-6n-NO_2 (**4a**)[b]	2.82	—	—	2.21	2.17	2.81	2.64	2.01	—	—	1.87	1.95	1.75	—
6n-Me-6x-NO_2 (**4b**)[d]	3.23	—	—	1.85	2.13	2.80	1.69	2.97	—	—	1.80		1.57	—
5x-Me-5n-NO_2 (**5a**)[b]	2.68	—	—	1.87	2.16	2.98	—	—	2.84	1.94	1.90	1.96	1.83	—
5n-Me-5x-NO_2 (**5b**)[b]	2.70	—	—	2.14	2.23	3.35	—	—	1.73	3.18	1.84[e]	1.81[e]	1.71	—
2x,3x-O, 5x-Me-5n-NO_2 (**6**)[d]	2.54	3.07[f]	—	3.14[f]	—	2.80	—	—	2.45	1.70	1.45	0.99	1.66	—

[a] Abbreviations: n = *endo*, x = *exo*, s = *syn*, a = *anti*. [b] Spectrum recorded at 500.135 MHz. [c] Designations n and x do not apply to these signals. [d] Spectrum recorded at 200.13 MHz. [e,f] Pairs of assignments may be interchanged.

values[18,19]) by substituent stereochemistry. Changes in chemical shifts (Δδ values) for pairs of isomers epimeric at a single centre, however, follow certain trends. Most striking is the through-space influence of the nitro group. For all pairs of isomers in which NO_2 and CH_3 are epimeric [*e.g.*, (**2a**) and (**2b**)], the vicinal nucleus 5-H (or 6-H) eclipsed by NO_2 is deshielded on average by 1.11 δ units relative to the vicinal H anticlinal to NO_2 (Δδ +1.11). Less impressively, *exo*-NO_2 groups deshield the synclinally-disposed vicinal bridgehead protons in the alcohols and ketones [but not the alkenes (**1**)] relative to the corresponding *endo*-NO_2 epimers, in which the bridgehead protons and NO_2 groups are nearly orthogonal (Δδ *ca.* +0.37). The boat or twist-boat conformation apparent in the norbornane skeleton also leads to 1,3-pseudo-diaxial interactions in which *endo*-NO_2 shields *endo*-H: the appropriate H (2n-H or 3n-H) in compounds of series **a** is shielded relative to the equivalent H in the epimer of series **b** (Δδ *ca.* −0.38). No significant shift results from interaction between *endo*-NO_2 and *endo*-H in a 1,4-pseudo-diaxial arrangement (|Δδ| <0.15); and the shielding of *syn*-7-H by *exo*-NO_2 is also unimportant (Δδ *ca.* −0.15). These observations are probably unexceptional in view of the anisotropy of the planar nitro group (in-plane deshielding, out-of-plane shielding).[20] However, to invoke NO_2 anisotropy is to imply that the rotational immobility of NO_2 in nitronorboranes, apparent in some solid-state structures we have determined,[2,3] must persist in solution, even though in general the barrier to rotation about the C–NO_2 bond is known to be very low.[21]

Trends in ^{1}H chemical shifts for isomers in which hydroxy group stereochemistry is varied are also observable. Most importantly, *exo*- or *endo*-OH shields whichever vicinal 3-H it eclipses (Δδ *ca.* −0.71). Other through-space effects are much smaller than those due to the nitro group with the exception of *exo*-OH to *syn*-7-H; the latter signal shows an average downfield shift of *ca.* 0.33 relative to its position in appropriate *endo*-OH isomers. Owing to the complexity of stereochemical effects on ^{13}C chemical shifts,[18] we make no attempt at this stage to look for trends among the data in Table 3.

One remaining result is worthy of mention. The 6-*endo*-nitro-2-*endo*-hydroxy compound (**7a**) is the only alcohol isomer described in this report to show spin-spin coupling of the OH signal (δ 1.53) to the *exo*-2-H ($^3J_{HCOH}$ 2.0 Hz). We have previously shown[2] that this sort of coupling is indicative of intramolecular OH · · · O_2N hydrogen bonding, which acts as a conformational lock on the OH group, thereby permitting the operation of the coupling mechanism. The magnitude of the coupling constant, interpreted in terms of Fraser's variant of the Karplus equation for H–C–O–H systems,[22] indicates a dihedral angle of 111° between 2-H and OH, a value not substantially different from the crystallographically determined value of 109° for a related 2-*endo*-OH-6-*endo*-NO_2 compound.[2]

Experimental

Routine measurements were on Kofler micro hot-stage (m.p.), Pye-Unicam SP3-300 (i.r. in KBr dispersion), AEI MS-9 and Varian MAT 212 (m.s.), and Bruker AC200 FT or WP500 (n.m.r.) spectrometers. T.l.c. was on pre-coated silica gel plates (Merck F254), and column chromatography on Merck silica gel (particle size 0.063—0.200 mm). Gas chromatograms were obtained on a Varian 3300 instrument with nitrogen as carrier gas and a bonded phase fused silica capillary column (25 m × 0.22 mm internal diam., BP20 phase, thickness 0.25 μm) supplied by Scientific Glass Engineering (Australia).

Diels–Alder Reaction of 2-Nitropropene and Cyclopentadiene.—2-Nitropropene[23] (14.11 g, 0.162 mmol), an excess of freshly cracked cyclopentadiene (43 ml, *ca.* 0.52 mol), and diethyl ether (30 ml) were kept at room temperature for 41 h. Solvent was removed under reduced pressure to give a mixture of two isomeric 5-methyl-5-nitrobicyclo[2.2.1]hept-2-enes (**1a**) and (**1b**) and cyclopentadiene dimer (30.44 g), the first two in a ratio of 85:15 (n.m.r., g.c.). A portion of the mixture (10 g) was separated by medium pressure chromatography on ICN Kieselgel Woelm (0.032—0.063 mm) packed into two LC Cheminert glass columns (a scrubber column, 12.5 × 165 mm, followed by the main column, 27 × 960 mm) with hexane–acetone mixtures as eluant under a pressure of 40 lbf in^{-2} to yield 5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*hept*-2-*ene* (**1a**) (6.63 g, effective yield 81.3%), 5-endo-*methyl*-5-exo-*nitrobicyclo*[2.2.1]-*hept*-2-*ene* (**1b**) (0.86 g, 10.5%), and an unseparated mixture of the two (0.66 g, 8.1%). Compound (**1a**): m.p. 68—69 °C (from ethanol–water) (Found: C, 63.0; H, 7.6; N, 9.25. $C_8H_{11}NO_2$ requires C, 62.7; H, 7.2; N, 9.1%), R_F (hexane–acetone, 40:1, v/v) 0.41; $\nu_{max.}$($CHCl_3$) 3 000, 1 531 (NO_2), 1 450, 1 388, and 1 356 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3. Compound (**1b**): m.p. 64—67 °C (from methanol) (Found: C, 62.4; H, 7.3; N, 8.9. $C_8H_{11}NO_2$ requires C, 62.7; H, 7.2; N, 9.1%), R_F (hexane–acetone, 40:1, v/v) 0.59; $\nu_{max.}$($CHCl_3$) 2 996, 1 525 (NO_2), 1 450, 1 380, and 1 346 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

Synthesis of Methylnitrobicyclo[2.2.1]*heptan*-2-exo-*ols.*—Borane–dimethyl sulphide complex (1 ml, 10 mmol) was added by syringe over 15 min to a stirred solution of the appropriate

Table 2. Selected proton-proton coupling constants, $|J|_{H,H}$ (Hz)[a,b]

	1,2x	1,6x	2n,3n	2n,3x	2n,7a	2x,3n	2x,3x	2x,6x	3n,3x	3n,7a	3x,4	3x,5x	4,5x	5n,5x	5n,7s	6n,6x	6n,7s	7s,7a
2-ene, 5x-Me-5n-NO_2 (**1a**)	3.1	3.5	—	—	—	—	5.7	—	—	—	2.9	—	—	—	—	13.3	3.4	9.2
5n-Me-5x-NO_2 (**1b**)	2.9	3.9	—	—	—	—	5.7	—	—	—	3.3	—	—	—	—	13.2	2.9	9.1
2x-OH, 6x-Me-6n-NO_2 (**2a**)	—	—	6.9	2.5?	4.1?	—	—	—	13.4	2.6	4.9	2.8	4.2	14.0	3.1	—	—	10.7
6n-Me-6x-NO_2 (**2b**)	—	—	6.7	?	?	—	—	—	12.0	2.0	3.7?	3.0	4.6	14.2	2.8?	—	—	8.3
5x-Me-5n-NO_2 (**3a**)	—	5.0	6.8	2.6	2.9?	—	—	—	14.4	2.9	4.2	—	—	—	—	14.5	3.1	10.8
5n-Me-5x-NO_2 (**3b**)	—	5.3	6.8	2.8	2.7?	—	—	—	14.5	2.7	4.8	—	—	—	—	14.8	2.7	11.0
2n-OH, 6x-Me-6n-NO_2 (**7a**)[c]	4.1	—	—	—	—	4.1	10.6	—	12.9	3.7	4.8	3.2	4.1	14.1	2.2	—	—	11.1
6n-Me-6x-NO_2 (**7b**)	4.7	—	—	—	—	4.8	10.6	—	12.9	3.2	4.9	2.7	4.9	14.3	2.7	—	—	11.0
5x-Me-5n-NO_2 (**8a**)	4.5	4.6	—	—	—	3.3	10.4	1.5	14.7	3.5	4.4	—	—	—	—	14.7	3.0	11.0
5n-Me-5x-NO_2 (**8b**)	4.2	4.9	—	—	—	3.0	10.0	1.2	14.0	2.8	5.1	—	—	—	—	14.5	1.9	—
2-one, 6x-Me-6n-NO_2 (**4a**)	—	—	—	—	—	—	—	—	16.9	?	3.7	2.2	4.5	14.1	3.0	—	—	11.4
6n-Me-6x-NO_2 (**4b**)[b]	—	—	—	—	—	—	—	—	18.0?	2.0?	4.8	3.0	5.0	14.4	?	—	—	—
5x-Me-5n-NO_2 (**5a**)	—	4.7	—	—	—	—	—	—	18.6	4.6	4.3	—	—	—	—	14.8	2.9	11.0?
5n-Me-5x-NO_2 (**5b**)	—	5.3	—	—	—	—	—	—	18.5	3.6	4.5	—	—	—	—	15.1	2.2	12.5?
2x,3x-O, 5x-Me-5n-NO_2 (**6**)	—	3.9	3.5	—	1.4?	—	—	—	—	1.4?	—	—	—	—	—	14.2	3.5	10.9

[a] Coupling constants for 1,7s, 1,7a, 4,7s, and 4,7a are invariably present, but their sizes (in the range 1.4—1.8 Hz) are usually not readily discerned and measured. Long-range coupling constants for 1,3x, 1,4, 1,5x, 2x,4, and 4,6x are sometimes present, but are usually too small (< 1 Hz) to measure accurately. [b] A dash(—) indicates that a coupling is absent; a question mark (?), that a coupling constant is uncertain or not clearly resolved. [c] $^3J_{2x\text{-}OH}$ *ca.* 2.0 Hz.

Table 3. ^{13}C Chemical shifts (ε, $CDCl_3$, p.p.m. from TMS) at 50.32 MHz

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	Me
2-ene, 5x-Me-5n-NO_2 (**1a**)[a]	42.0	138.8	134.0	52.2	95.6	38.4	47.8	28.3
5n-Me-5x-NO_2 (**1b**)[a]	42.3	140.8	132.4	52.1	96.5	39.0	48.7	26.0
2x-OH, 6x-Me-6n-NO_2 (**2a**)[a]	55.5	69.5	39.9	35.7	39.4	93.0	34.3	28.4
6n-Me-6x-NO_2 (**2b**)	54.1	68.9	40.5	36.2	42.0	94.1	34.2	23.7
5x-Me-5n-NO_2 (**3a**)	44.4	72.1	36.9	47.3	94.6	36.1	33.9	27.9
5n-Me-5x-NO_2 (**3b**)	45.0	72.9	35.2	45.9	95.2	38.1	33.9	23.7
2n-OH, 6x-Me-6n-NO_2 (**7a**)	52.4	72.5	37.5	36.9	40.0	91.7	37.3	30.5
6n-Me-6x-NO_2 (**7b**)	50.9	72.5	37.0	36.8	43.7	97.0	37.2	25.9
5x-Me-5n-NO_2 (**8a**)	42.7	69.9	34.8	48.7	95.8	31.9	36.7	28.5
5n-Me-5x-NO_2 (**8b**)	43.1	70.6	33.3	47.2	96.0	32.9	37.0	23.1
2-one, 6x-Me-6n-NO_2 (**4a**)[a]	61.3	210.6	43.1	35.1	40.9	92.6	37.8	26.1
6n-Me-6x-NO_2 (**4b**)	60.5	212.1	44.1	35.1	42.0	91.4	37.2	25.5
5x-Me-5n-NO_2 (**5a**)	49.7	212.8	40.8	46.7	93.9	35.9	36.5	28.3
5n-Me-5x-NO_2 (**5b**)	50.3	213.2	39.2	45.4	94.1	37.3	36.5	23.8
2x,3x-O, 5x-Me-5n-NO_2 (**6**)	37.1	48.2[b]	49.7[b]	46.9	95.7	37.1	25.0	28.4

[a] Spectrum recorded at 125.76 MHz. [b] Assignments may be interchanged

nitrobicyclo[2.2.1]hept-2-ene (**1a**) or (**1b**) (*ca.* 10 mmol) in dry tetrahydrofuran (10—25 ml) at room temperature under a nitrogen atmosphere. After 5—8 h, aqueous sodium hydroxide (3M; 2 ml) was added dropwise, followed by hydrogen peroxide (30%; 2 ml). The mixture was stirred at room temperature for 18—38 h, after which the organic solvent was removed under reduced pressure. Water (25 ml) was added, and the mixture was extracted with ether (3 × 40 ml). The combined extracts were washed with water and saturated brine, dried (K_2CO_3), and evaporated under reduced pressure. The crude product was separated by column chromatography on silica gel with hexane–ethyl acetate mixtures as eluant.

From 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]hept-2-ene (**1a**) (1.58 g, 10.3 mmol) were obtained recovered starting material (**1a**) (15 mg, 1%); 6-exo-*methyl*-6-endo-*nitrobicyclo*[2.2.1]*heptan*-2-exo-*ol* (**2a**) (0.94 g, 53%), m.p. 90—91 °C (from benzene–hexane) (Found: C, 56.4; H, 7.7; N, 8.0. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 3:1, v/v) 0.28; $\nu_{max.}$($CHCl_3$) 3 600 and 3 440br (OH), 2 980, 1 530, and 1 350 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3; *m/z* 125 (2%, $M^+ - NO_2$), 95 (36), 82 (100), 80 (24), and 79 (26); and 5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*heptan*-2-exo-*ol* (**3a**) (0.32 g, 18%), m.p. 64—65 °C (from chloroform–hexane) (Found: C, 56.2; H, 8.0; N, 8.2. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 3:1, v/v) 0.09; $\nu_{max.}$($CHCl_3$) 3 620 and 3 480br (OH), 2 990, 1 512, and 1 333 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

From 5-*endo*-methyl-5-*exo*-nitrobicyclo[2.2.1]hept-2-ene (**1b**) (1.53 g, 10.0 mmol) were obtained 6-endo-*methyl*-6-exo-*nitrobicyclo*[2.2.1]*heptan*-2-exo-*ol* (**2b**) (560 mg, 44%) as an oil; R_F (hexane–ethyl acetate, 1:1, v/v) 0.28; $\nu_{max.}$($CHCl_3$) 3 600 and 3 450br (OH), 2 970, 1 535, and 1 350 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3 (Found: $M^+ - NO_2$, 125.0967. $C_8H_{13}O$ requires 125.0966); and 5-endo-*methyl*-5-exo-*nitrobicyclo*[2.2.1]*heptan*-2-exo-*ol* (**3b**) (170 mg, 14%), m.p. 73—74 °C (from di-isopropyl ether–hexane) (Found: C, 55.85; H, 7.7; N, 8.0. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 1:1, v/v) 0.20; $\nu_{max.}$($CHCl_3$) 3 620 and 3 450br (OH), 2 980, 1 530, and 1 350 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

Oxidations with Dimethyl Sulphoxide–Oxalyl Chloride.—Dry dimethyl sulphoxide (2.4 ml, *ca.* 34 mmol) was added by syringe to a stirred solution of oxalyl chloride (1.0 ml, *ca.* 11 mmol) in dry dichloromethane (20 ml) kept at −63 °C under nitrogen. After 2 min, a solution of the appropriate *exo*-alcohol (1.00 g, 5.83 mmol) in dry dichloromethane (5 ml) was added over 2 min by syringe, followed, after a further 2 min, by dry triethylamine (2.4 ml, *ca.* 17 mmol). The mixture was allowed to warm to room temperature, and then stirred for 17.5 h. Water (60 ml) was added, and the layers were separated. The aqueous phase was extracted with dichloromethane (3 × 20 ml). The combined organic layers were washed with saturated brine, dried ($MgSO_4$), and evaporated under reduced pressure. The crude ketone was purified by column chromatography on silica gel with hexane–ethyl acetate mixtures as eluant.

From 6-*exo*-methyl-6-*endo*-nitrobicyclo[2.2.1]heptan-2-*exo*-ol (**2a**) was obtained 6-exo-*methyl*-6-endo-*nitrobicyclo*[2.2.1]-*heptan*-2-*one* (**4a**) (780 mg, 79%), m.p. 114—116 °C (from ethyl acetate) (Found: C, 56.5; H, 7.0; N, 8.3. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%), R_F (hexane–ethyl acetate, 1:1, v/v) 0.46; $\nu_{max.}$($CHCl_3$) 3 000, 1 760 (CO), and 1 550 and 1 360 cm^{-1} (NO_2): δ_H and δ_C, see Tables 1—3; *m/z* 169 (6%, M^+), 123 (56, $M^+ - NO_2$), 95 (87), 93 (55), 81 (100), 79 (66), 77 (43), and 67 (77).

From 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]heptan-2-*exo*-ol (**3a**) was obtained 5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*heptan*-2-*one* (**5a**) (0.84 g, 85%), m.p. 117—118 °C (from ethyl acetate) (Found: C, 56.3; H, 6.5; N, 8.1. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%), R_F (hexane–ethyl acetate; 1:1, v/v) 0.45; $\nu_{max.}$($CHCl_3$) 3 000, 1 754 (CO), and 1 538 and 1 360 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3; *m/z* 123 (42%, $M^+ - NO_2$), 95 (100), 93 (45), 83 (47), 81 (62), 79 (53), and 67 (66).

Oxidations with Ruthenium Tetraoxide.—A mixture of the appropriate 2-*exo*-alcohol (1 mmol), acetonitrile (2 ml), tetrachloromethane (2 ml), water (3 ml), sodium periodate (3 mmol) and a catalytic quantity of hydrated ruthenium dioxide (*ca.* 3 mg) was stirred vigorously at room temperature until t.l.c. indicated that the starting material was consumed (43—58 h). Propan-2-ol (10 ml) and water (30 ml) were added, and stirring was continued for a few minutes. The mixture was extracted with several portions of dichloromethane, and the combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography with hexane–ethyl acetate mixtures as eluant.

From 6-*exo*-methyl-6-*endo*-nitrobicyclo[2.2.1]heptan-2-*exo*-ol (**2a**) (171 mg, 1 mmol) was obtained 6-exo-*methyl*-6-endo-*nitrobicyclo*[2.2.1]*heptan*-2-*one* (**4a**) (120 mg, 73%); characterisation as above.

From 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]heptan-2-*exo*-ol (**3a**) (428 mg, 2.50 mmol) was obtained 5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*heptan*-2-*one* (**5a**) (340 mg, 79%); characterisation as above.

From 6-*endo*-methyl-6-*exo*-nitrobicyclo[2.2.1]heptan-2-*exo*-

ol (**2b**) (208 mg, 1.22 mmol) was obtained 6-endo-*methyl*-6-exo-*nitrobicyclo*[2.2.1]*heptan*-2-*one* (**4b**) (170 mg, 88%), m.p. 73—74 °C (sealed tube; from ethyl acetate, then sublimation) (Found: C, 56.6; H, 6.6; N, 8.3. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%), R_F (hexane–ethyl acetate, 3:1, v/v) 0.43; $\nu_{max.}$($CHCl_3$) 3 100, 1 750 (CO), and 1 540 and 1 350 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

From 5-*endo*-methyl-5-*exo*-nitrobicyclo[2.2.1]heptan-2-*exo*-ol (**3b**) (127 mg, 0.74 mmol) was obtained 5-endo-*methyl*-5-exo-*nitrobicyclo*[2.2.1]*heptan*-2-*one* (**5b**) (90 mg, 72%), m.p. 61—62 °C (sealed tube; after sublimation) (Found: C, 56.2; H, 6.7; N, 8.3. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%), R_F (hexane–ethyl acetate, 3:1, v/v; 0.31, $\nu_{max.}$($CHCl_3$) 3 195, 1 750 (CO), and 1 535 and 1 390 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

Reductions with K-Selectride.—Potassium tri-s-butylborohydride (K-selectride; 0.5M, 3 ml, 1.5 mmol) was added by syringe to a stirred solution of the appropriate ketone (1 mmol) in dry tetrahydrofuran (5 ml) under nitrogen at 0—5 °C. Stirring was maintained at this temperature for 1 h, and then at room temperature for 20—60 h. The solvent was removed under reduced pressure, and the crude product was stirred with aqueous hydrochloric acid (2M; 20 ml) for 1 h. The mixture was extracted with several portions of dichloromethane, after which the extracts were washed with saturated brine, dried ($MgSO_4$), and evaporated under reduced pressure. If n.m.r. showed the presence of s-butyl residues in the product, the hydrolysis was repeated at *ca.* 40 °C for longer periods, or with the addition of ethanol as co-solvent. The crude product (**7a**) was purified by recrystallisation, while (**8a**) was purified by column chromatography on silica gel with hexane–ethyl acetate mixtures as eluant.

From 6-*exo*-methyl-6-*endo*-nitrobicyclo[2.2.1]heptan-2-one (**4a**) (349 mg, 2.06 mmol) was obtained 6-exo-*methyl*-6-endo-*nitrobicyclo*[2.2.1]*heptan*-2-endo-*ol* (**7a**) (232 mg, 66%), m.p. 96—97 °C (from ethyl acetate, then hexane–chloroform) (Found: C, 56.1; H, 7.6; N, 8.1. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 1:1, v/v) 0.54; $\nu_{max.}$($CHCl_3$) 3 600 and 3 440br (OH), 2 960, 1 530, and 1 350 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3; *m/z* 125 (4%, $M^+ - NO_2$), 95 (53), 85 (27), 83 (40), 81 (100), 79 (51), and 67 (29).

From 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]heptan-2-one (**5a**) (178 mg, 1.05 mmol) was obtained 5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*heptan*-2-endo-*ol* (**8a**) (73 mg, 41%), m.p. 97—98 °C (from hexane–chloroform) (Found: C, 56.7; H, 7.6; N, 8.2. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 1:1, v/v) 0.44; $\nu_{max.}$($CHCl_3$) 3 600 and 3 500br (OH), 2 980, 1 530, and 1 354 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

Reductions with Sodium Borohydride.—Sodium borohydride (0.5 mmol) was added to a stirred solution of the appropriate ketone (*ca.* 0.45 mmol) in methanol (2.5 ml) at 0—5 °C. Stirring was maintained at this temperature for 10—20 min, and at room temperature for 1.3—2 h. Solvent was removed under reduced pressure, after which water (10 ml) and dilute hydrochloric acid (2M; 5 ml) were added to the residue. The mixture was extracted with ether (3 × 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Products were purified by column chromatography on silica gel with hexane–ethyl acetate mixtures as eluant.

From 6-*endo*-methyl-6-*exo*-nitrobicyclo[2.2.1]heptan-2-one (**4b**) (72 mg, 0.43 mmol) was obtained 6-endo-*methyl*-6-exo-*nitrobicyclo*[2.2.1]*heptan*-2-endo-*ol* (**7b**) (68 mg, 93%) as an oil; R_F (hexane–ethyl acetate, 1:1, v/v) 0.63; $\nu_{max.}$($CHCl_3$) 3 606 and 3 300br (OH), 2 800, 1 540, and 1 300 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3 (Found: $M^+ - NO_2$, 125.0967. $C_8H_{13}N$ requires 125.0966).

From 5-*endo*-methyl-5-*exo*-nitrobicyclo[2.2.1]heptan-2-one (**5b**) (80 mg, 0.47 mmol) was obtained 5-endo-*methyl*-5-exo-*nitrobicyclo*[2.2.1]*heptan*-2-endo-*ol* (**8b**) (76 mg, 95%). Further purification gave needles (55 mg, 68%), m.p. 83—84 °C (sealed tube; from hexane–dichloromethane) (Found: C, 56.4; H, 7.7; N, 8.2. $C_8H_{13}NO_3$ requires C 56.1; H, 7.65; N, 8.2%), R_F (hexane–ethyl acetate, 1:1, v/v) 0.30; $\nu_{max.}$($CHCl_3$) 3 725 and 3 450br (OH), 3 075, 1 590, and 1 435 cm^{-1} (NO_2); δ_H and δ_C, see Tables 1—3.

2,3-exo-*Epoxy*-5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]-*heptane* (**6**).—A solution of *m*-chloroperoxybenzoic acid (54% pure; 990 mg, *ca.* 3.1 mmol) in dichloromethane (45 ml) was added dropwise to a stirred solution of 5-*exo*-methyl-5-*endo*-nitrobicyclo[2.2.1]hept-2-ene (**1a**) (249 mg, 1.62 mmol) in dichloromethane (5 ml) in which was suspended anhydrous disodium hydrogen phosphate (1.09 g). Stirring was maintained at room temperature for 33 h. The mixture was washed with aqueous sodium metabisulphite, and the organic phase was evaporated under reduced pressure. The residue was dissolved in ether, which was washed with aqueous sodium hydrogen carbonate (3 × 30 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The chromatographically pure 2,3-exo-*epoxy*-5-exo-*methyl*-5-endo-*nitrobicyclo*[2.2.1]*heptane* (**6**) (250 mg, 91%) so obtained was further purified by recrystallisation to give prisms (152 mg, 55%), m.p. 99—101 °C (from di-isopropyl ether) (Found: C, 56.4; H, 6.6; N, 8.1. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%), R_F (hexane–ethyl acetate, 3:1) 0.79; $\nu_{max.}$($CHCl_3$) 3 010, 2 910, 1 542, and 1 365 (NO_2), and 830 cm^{-1} (epoxide); δ_H and δ_C, see Tables 1—3.

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