Stereochemistry of Ring Enlargements with Bridged Systems. Comparison of the Nitrous Acid Deamination of *endo*- and *exo*-2-Aminomethylbicyclo[3.2.1]octan-2-ol with the Reaction between Bicyclo[3.2.1]-octan-2-one and Diazomethane [1]

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The synthesis and nitrous acid deamination of *exo*- and *endo*-2-aminomethylbicyclo[3.2.1]octan-2-ol are described. The product distribution is markedly dependent on the amino-alcohol stereochemistry and comparison with the product distribution for the diazomethane ring enlargement of bicyclo[3.2.1]octan-2-one suggests that diazomethane attacks the carbonyl group preferentially from the *exo*-side (equatorial direction). A similar study with bicyclo[2.2.1]heptane systems is also reported.

RECENTLY there has been considerable interest in the reactions of bridged ketones {norcamphor (norbornan-2-one) and its higher homologues,[2a] bicyclo[2.1.1]hexan-2-one,[2b] diamantanone,[2c] and bicyclo[3.3.1]nonan-9-one [2d]} with diazomethane and of bridged amino-alcohols (derived from homoadamantan-4-one [3a] or norcamphor [3b]) with nitrous acid, for the synthesis of higher homologous systems.

Whilst some of these reactions do not involve stereochemical problems either at the amino-alcohol centre [3a] or as to the direction of approach of diazomethane to the carbonyl group,[2b-d] such problems are generally expected. They have been met in the other cases above [2a,3b] and it has been shown that the product composition for deamination of the epimeric amino-alcohols derived from norcamphor depends strongly on the stereochemistry at the amino-alcohol centre.[3b]

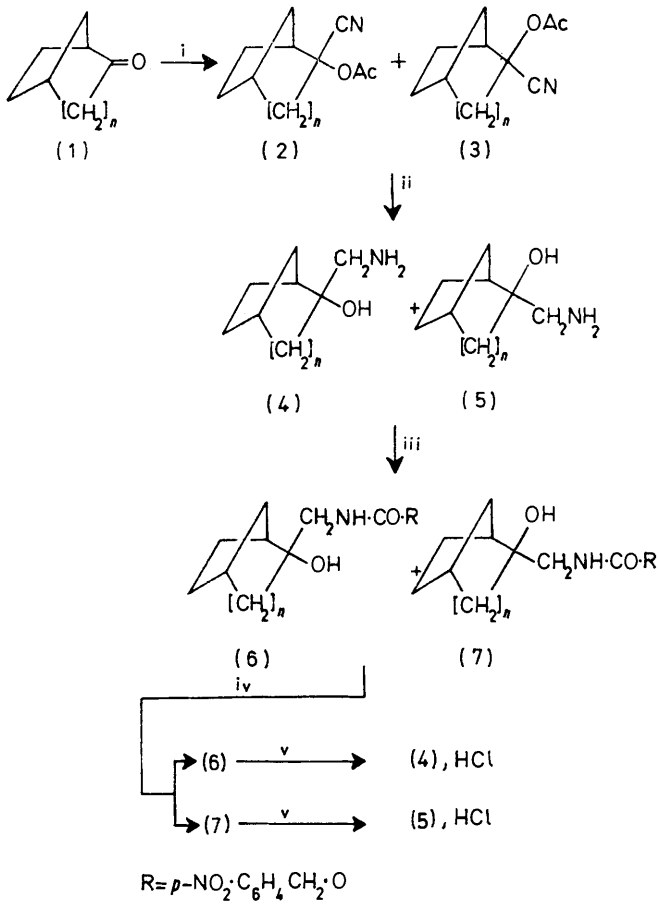
We report here a stereochemical study of the homologation of the bicyclo[3.2.1]octane system to the bicyclo-[4.2.1]nonane system and full experimental details are also reported for a previous study of the homologation of the bicyclo[2.2.1]heptane system to the bicyclo-[3.2.1]octane system.[3b]

RESULTS AND DISCUSSION

The amino-alcohols (4) and (5) ($n = 1$ or 2) required for homologation were synthesised starting from the cyanohydrin reaction of the parent ketones (Scheme 1). G.l.c. analysis of the acetylation mixture from the reaction of norcamphor showed two poorly separated peaks with ratio of areas 75 : 25. The ^{1}H n.m.r. spectrum showed two methyl signals at δ 2·14 and 2·07 whose ratio of areas was about the same as for the chromatographic peaks, thus pointing to a mixture of (2) and (3) ($n = 1$). Similar observations were made with the reaction of bicyclo[3.2.1]octan-2-one. Here, the minor chromatographic peak was merely a shoulder, but again two methyl peaks, in a *ca.* 65 : 35 ratio, were seen at δ 4·20 and 4·28.

Because the cyanohydrin acetates proved so difficult to separate, they were reduced to the amino-alcohols, which were again shown to be a mixture of *endo*- and *exo*-aminomethyl-isomers, in about the ratio given above, by their ^{1}H n.m.r. aminomethylene signals.

The amino-alcohols from norcamphor [(4) and (5); $n = 1$] proved to be very unstable and, moreover, were



SCHEME 1 *Reagents:* i, *a* HCN, *b* Ac_2O–AcCl; ii, $LiAlH_4$; iii, RCO-Cl–C_6H_5N–dioxan; iv, fractional crystallisation from C_6H_6; v, *a* H_2/Pd–C, *b* HCl–Et_2O.

strongly adsorbed on g.l.c. columns. However, protection of the amino-group with *p*-nitrobenzyl chloroformate gave a stable, crystalline material which, again, showed two different methylene signals, with the ratio of areas given above for both the (2)—(3) and (4)—(5) ($n = 1$) mixtures. In our hands t.l.c. failed to separate

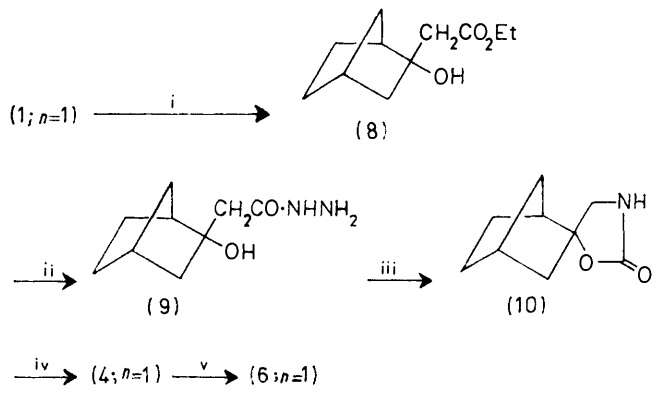
[1] Based in part on the doctoral thesis of E. Volpi, Pisa, 1972.

[2] (*a*) G. Fachinetti, F. Pietra, and A. Marsili, *Tetrahedron Letters*, 1971, 393; (*b*) T. Gibson, *J. Org. Chem.*, 1972, **37**, 700; (*c*) I. Tabushi, Y. Aoyama, N. Takahashi, T. M. Gund, and P. v. R. Schleyer, *Tetrahedron Letters*, 1973, 107; (*d*) N. J. Leonard and J. C. Coll, *J. Amer. Chem. Soc.*, 1970, **92**, 6685.

[3] (*a*) T. Sasaki, S. Eguchi, T. Toru, and K. Itoh, *J. Amer. Chem. Soc.*, 1972, **94**, 1357; (*b*) E. Volpi and F. Pietra, *Tetrahedron Letters*, 1972, 4867.

the two isomers, whilst fractional crystallisation from benzene was successful. We have collected only the less soluble (7; $n = 1$) of the two isomers by this route. The other isomer (6; $n = 1$) was easily synthesised by the route shown in Scheme 2, which served also to establish the stereochemistry: the organozinc reagent is expected to lead to *exo*-attack, in accordance with the stereochemistry for the reaction of norcamphor with Grignard reagents,[4] and this identifies the predominant cyanohydrin acetate as the epimer (2; $n = 1$).

Attempts to prepare (4; $n = 1$) by the reaction of norcamphor with nitromethane (a standard method for the homologation of cyclohexanone [5]) were unsuccessful, and under a variety of conditions we recovered all the starting ketone. This was not expected because norcamphor is only ten times less reactive than cyclohexanone towards sodium borohydride, the latter reacting rapidly.[6]



SCHEME 2 *Reagents:* i, $BrCH_2{\cdot}CO_2Et$–Zn–C_6H_6–C_6H_5Me; ii, N_2H_4,H_2O–EtOH; iii, HNO_2; iv, NaOEt–EtOH; v, RCO·Cl–C_6H_5N–dioxan.

Conversion of the oxazolidone (10) into (4; $n = 1$) had to be carried out in alkali. Under the usual, acidic conditions,[7] a different, uninvestigated, crystalline material was obtained, probably owing to further reaction of (4; $n = 1$), as a tertiary alcohol, in the acidic medium.

Because the reaction of bicyclo[3.2.1]octan-2-one with methylmagnesium compounds was already known to be scarcely stereoselective, giving a nearly 1 : 1 mixture of the *exo*- and *endo*-carbinols,[6] we decided to isolate both (6) and (7) ($n = 2$) by fractional crystallisation. Again, ^1H n.m.r. spectra revealed two different *N*-methylenes pointing to a mixture of (6) + (7) ($n = 2$) in the ratio expected from both the chromatography and the ^1H n.m.r. spectra of their precursors (see above). In one of the two epimers the *N*-methylene was seen as an AB quartet, further split by coupling with the amide proton. With the other isomer, only coupling with the amide proton was observed, and thus the signal for the *N*-methylene appeared as a doublet which changed into a singlet on the shaking with D_2O.

Hydrogenolysis of the derivatives (6) and (7) on Pd–C was rapid and the amino-alcohols were collected as hydrochlorides.

Product distributions for the reactions of bridged amino-alcohols with nitrous acid and of the corresponding ketones with diazomethane

	Product distribution [a]	
	Bicyclo[4.2.1]nonanones	
Reaction	3-oxo	2-oxo
(4; $n = 2$) + HNO_2	0·13 (5)	1 (65)
(5; $n = 2$) (~90%) + (4; $n = 2$) (~10%) + HNO_2	0·97 (39·0)	1 (38·1)
(5; $n = 2$) + HNO_2	~0·92 [b]	1
(1; $n = 2$) + CH_2N_2 (0·06 equiv.)	0·48 [c]	1
	Bicyclo[3.2.1]octanones	
	3-oxo	2-oxo
(4; $n = 1$) + HNO_2	0·40 (20·0) [d]	1 (51·4) [d]
(5; $n = 1$) (~82%) + (4; $n = 1$) (~18%) + HNO_2	0·05 (2·9) [d]	1 (57·3) [d]
(5; $n = 1$) + HNO_2	~0 [d]	1 [d]
(1; $n = 1$) + CH_2N_2 (0·06 equiv.)	0·40 [d]	1 [d]

[a] Actual yields(%) are given in parentheses. [b] Value extrapolated for reaction of pure (5; $n = 2$) on the basis of the above data for pure (4; $n = 2$) and for the (5; $n = 2$) + (4; $n = 2$) mixture of known composition. [c] Corrected for a very small amount of the next higher homologous ketones. [d] From reference 3*b*.

The product distributions from the deaminations of the amino-alcohols (4) and (5) are shown in the Table, together with the product distribution for the reactions of ketones (1) ($n = 1$ or 2) with diazomethane. The latter reactions were carried out in methanol with a large excess of ketone in order to minimise reactions of ring-enlarged ketones with diazomethane. These could not be entirely avoided, however, so that corrections were made in order that the data in the Table represent the true ratio of isomeric ketones from ring enlargement reactions.

It is apparent from the Table that the ratio of isomeric ketones from the reaction of norcamphor (1; $n = 1$) with diazomethane is nearly identical with that obtained in the deamination of the *exo*-aminomethyl compound (4; $n = 1$), while the isomeric *endo*-aminomethyl compound gave only one of the two ring-enlarged ketones. As discussed previously,[3b] this points to predominant, if not exclusive, *exo*-attack by diazomethane on (1; $n = 1$).

Considering the bicyclo[3.2.1]octane system, it is clear from the Table using the same criterion as above,[3b] that diazomethane attacks (1; $n = 2$) from both faces of the carbonyl group since both ring-enlarged ketones are formed from either (4) or (5) ($n = 2$). However, because the ratio of ring-enlarged ketones from the reaction with diazomethane is not just the mean of the ratios observed for deaminations of amino-alcohols, it is clear that diazomethane has a preferred direction of attack on (1; $n = 2$).

Because (1; $n = 2$) can be treated as a substituted cyclohexanone system,[6] and it has been shown that

[4] W. Kraus, *Annalen*, 1965, **685**, 97.
[5] J. Dauben, *Org. Synth.*, Coll. Vol. IV, 1963, p. 221.
[6] E. Volpi, G. Biggi, and F. Pietra, *J.C.S. Perkin II*, 1973, 571.
[7] H. Walters, *J. Biol. Chem.*, 1949, **121**, 181; J. Namirovski, *J. prakt. Chem.*, 1885, **31**, 173; A. F. McKay and R. O. Braun, *J. Org. Chem.*, 1951, **16**, 1829.

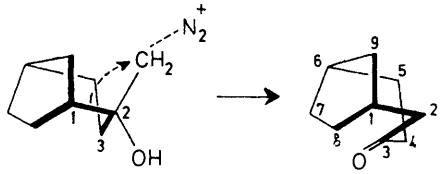
diazomethane attacks other substituted (steroidal [8a] or decalones [8b]) cyclohexanones preferentially from the equatorial side, it follows that the amino-alcohol which, on deamination, gives the product distribution more closely resembling that from the reaction of (1; $n = 2$) with diazomethane should have the hydroxy-group in the axial direction. This deduction is in accordance with accepted spectral criteria of configurational assignment in cyclohexanols.[9a] In fact, (5) and (4) ($n = 2$) show strong i.r. absorptions at 1097 and 1120 cm^{-1}, respectively, which can be attributed to the C–O stretching mode. It is unfortunate that this assignment cannot be further substantiated by the examination of the same stretching mode for the alcohol acetates, which is a standard criterion with cyclohexanols.[9a]

Moreover, assuming that acetylation has not altered the original composition of the mixture of cyanohydrins from (1; $n = 2$), which is an acceptable assumption as acetylations are usually rapid reactions, the above stereochemical assignment is also in accordance with known conformational energy values in cyclohexane systems which are slightly higher for OH than CN groups.[9b]

The stereochemistry of diazomethane attack on the cyclohexanone system (1; $n = 2$) can be compared with that for attack of a Grignard reagent, methylmagnesium iodide, on the same system.[6] In the latter case a near 1 : 1 ratio for equatorial *vs.* axial attack was observed, whereas with diazomethane, if the above conclusions are correct, equatorial attack greatly predominates.

The ' size ' of the nucleophilic reagents can hardly be responsible for the observed stereochemistry. If anything, it is the strongly associated Grignard reagent which is expected to be the larger and, on this basis, it would have been expected to seek preferentially for the less sterically demanding equatorial direction. However, an acceptable rationale for the observed stereochemistry can be derived from a consideration of the position of transition states along the reaction co-ordinate. We have already argued that attack at the carbonyl group should occur with an early transition state for Grignard reagents and with a late transition state for diazomethane.[6,10] If this is the case, diazomethane, approaching closer to the carbonyl carbon in the rate-limiting transition state than the Grignard reagent does, gives rise to a comparatively more crowded transition state around the reaction centre. Consequently, diazomethane seeks, preferentially, for the less sterically hindered direction (equatorial) of attack.

The migratory aptitudes in deamination of (4) and (5) ($n = 1$) have already been discussed.[3b] Molecular models clearly indicate that even with (4) and (5) ($n = 2$) the migratory aptitudes for formation of ring-enlarged ketones cannot be accounted for on the basis of ground state conformations, unlike the case of the reactions of cyclopropanones with diazoalkanes.[11] A possible explanation for the results of the deamination of (4; $n = 2$) is that during the migration of the C(1)–C(2) bond (Scheme 3) interactions arise between the developing C(8) and C(3) atoms of the product.



SCHEME 3

Thus, migration of the C(3)–C(2) bond, which, according to molecular models, cannot involve any strong steric compression, is preferred despite the adverse electronic factor [*i.e.* on purely electronic grounds migration of the tertiary C(1) would be expected to prevail over that of the secondary C(3)].

With (5; $n = 2$), according to electronic factors, a slight preference for migration of the tertiary carbon was expected.[12] Actually, preferential migration of the secondary carbon, albeit to a very slight extent, was observed (Table). The energy differences involved are small, and rationalisation of these observations is difficult.

Finally, our results for the reaction of (1; $n = 2$) with anhydrous hydrogen cyanide cast some doubt on the claim [13] that the reaction of the same ketone with hydrogen cyanide generated *in situ* from potassium cyanide and sulphuric acid gives a single cyanohydrin (to which the configuration with equatorial CN group was tentatively assigned [13]). This claim was based on the observation of a single g.l.c. peak for the acetylation product, while we have shown above that (2) and (3) ($n = 2$) are very difficult to separate. Therefore we suggest that this cyanohydrin reaction in aqueous medium [13] should be re-examined before the conclusions of Vaughan *et al.*[13] are accepted.

EXPERIMENTAL

^{1}H N.m.r. spectra were obtained with either a Varian A60 or a JEOL SP 100 spectrometer and data are given in δ, with respect to Me_4Si as internal standard. I.r. spectra were recorded on a Perkin-Elmer 337 grating spectrophotometer.

Mixture of exo- (2; $n = 1$) *and* endo-2-*Cyanobicyclo*-[2.2.1]*heptan*-2-*yl Acetate* (3; $n = 1$).—To a cooled (−70°) mixture of (1; $n = 1$) (19·2 g), potassium cyanide (0·05 g), and dried diethylamine (2 drops) was added dried HCN [14]

[8] (*a*) J. B. Jones and P. Price, *Chem. Comm.*, 1969, 1478; (*b*) R. G. Carlson and N. S. Behn, *J. Org. Chem.*, 1968, **33**, 2069.

[9] (*a*) E. A. Braude and E. S. Waight, in ' Progress in Stereochemistry,' ed. W. Klyne, Butterworths, London, vol. I, 1954, pp. 126—176; (*b*) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, ' Conformational Analysis,' Interscience, New York, 1965, pp. 44 and 118.

[10] In reference 6, p. 574, right-hand column, lines 18—19, read ' former ' for ' latter ' and *vice versa*. The two terms were inverted owing to a misprint.

[11] N. J. Turro and R. G. Gagosian, *J. Amer. Chem. Soc.*, 1970, **92**, 2036.

[12] H. O. House, E. J. Grubb, and W. F. Gannon, *J. Amer. Chem. Soc.*, 1960, **82**, 4099.

[13] W. R. Vaughan and R. Caple, *J. Amer. Chem. Soc.*, 1964, **86**, 4928.

[14] Houben-Weil, ' Methoden der Organischen Chemie,' G. Thieme Verlag, Stuttgart, 1952, pp. 255—256. We emphasise that it is necessary to maintain the temperature of the reaction flask over 80° in order to have quick evolution of hydrogen cyanide; this is not indicated in K. Ziegler, *Org. Synth.* Coll. Vol. I, 1951, p. 314.

(14 ml) with protection from moisture. After 24 h at 0—4° under stirring, dried ether (15 ml), phosphoric acid (0·04 ml), acetic anhydride (30 ml), and acetyl chloride (1·5 ml) were successively added with protection from moisture. After 2 days at 0° and an additional 2 days at room temperature under stirring, the mixture was evaporated and then distilled at 83° and 0·15 mmHg to give a *ca.* 75 : 25 (see text) mixture of (2) and (3) (n = 1) (25 g, 73%) (Found: C, 66·9; H, 7·3; N, 8·2. Calc. for $C_{10}H_{13}NO_2$: C, 67·1; H, 7·3; N, 7·9%), $\nu_{max.}$ 2250s and 1760vs cm^{-1}.

endo-2-p-*Nitrobenzamidomethylbicyclo*[2.2.1]*heptan*-2-*ol* (7; n = 1).—To a solution of the foregoing mixture of (2) and (3) (n = 1) (5 g) in dried ether (25 ml), was added, under vigorous stirring and protection from mixture, over 0·5 h a solution of $LiAlH_4$ (3 g) in ether (150 ml). After 1 h at reflux the $LiAlH_4$ in excess was destroyed,[15] the ethereal layer evaporated, and the residue distilled at 80° and 1 mmHg to give a *ca.* 75 : 25 (see text) mixture of (4) and (5) (n = 1) (3 g, 75%) (Found: C, 68·4; H, 10·7; N, 10·0. Calc. for $C_8H_{15}NO$: C, 68·5; H, 10·7; N, 9·9%). This mixture was very unstable to air, rapidly giving an unidentified crystalline solid, but was quite stable under N_2. To a stirred, ice-cooled solution of the foregoing mixture of (4) and (5) (n = 1) (5·5 g) in dried dioxan (20 ml) were separately added, in 1·5 h under N_2, *p*-nitrobenzyl chloroformate [16] and dried pyridine (3·5 ml). The mixture was then heated at 65° for 12 h, cooled, and, after the addition of water (25 ml), thoroughly extracted with chloroform. The chloroform extract was evaporated to dryness, the residue was dissolved in benzene (20 ml), and then, by addition of n-pentane (10 ml) a crystalline mixture of (6) and (7) (n = 1) was obtained (9·5 g, 76%). A sample (8 g) of this mixture was fractionally recrystallised from benzene. After ten recrystallisations the endo-*isomer* (7; n = 1), m.p. 152—154°, was obtained as the less soluble fraction (0·25 g) (Found: C, 60·0; H, 6·3; N, 8·5. $C_{16}H_{20}N_2O_5$ requires C, 60·0; H, 6·3; N, 8·7%), δ ($CDCl_3$) 8·3, 8·1, 7·6, and 7·4 (4H, ABX system), 5·4br (1H), 5·2 (2H, s), 3·35 (2H, d, J 6 Hz), 2·4—0·6 (11H); a sharp absorption emerging at 2·08 disappeared on the shaking with D_2O.

endo-2-*Aminomethylbicyclo*[2.2.1]*heptan*-2-*ol* (5; n = 1).—The compound (7; n = 1) (0·07 g) was hydrogenolysed in absolute ethanol (10 ml) on 20% Pd–C until it had absorbed 24 ml of H_2. The mixture was then filtered and the filtrate was concentrated nearly to dryness under reduced pressure. The residue was dissolved in dried ether and then dried gaseous HCl was bubbled through for a few minutes to precipitate (5; n = 1) as the hydrochloride in nearly quantitative yield. The free *amino-alcohol* (5; n = 1) was liberated with sodium hydrogen carbonate, extracted with chloroform, and distilled at 80° and 1 mmHg (Found: C, 68·5; H, 10·6; N, 9·9. $C_8H_{15}NO$ requires C, 68·5; H, 10·7; N, 9·9%), δ ($CDCl_3$) 2·76 (ABq), 2·4 (3H, s, exch. D_2O), and 2·4—0·9 (10H).

exo-2-*Carbazoylmethylbicyclo*[2.2.1]*heptan*-2-*ol* (9).—To a mixture of granular zinc (12 g) and dried 1 : 1 benzene–toluene (20 ml), at 100° under stirring and with protection from atmosphere, was added a solution of dried 1 : 1 benzene–toluene (40 ml), ethyl bromoacetate (37·5 ml), and norbornan-2-one (16·4 g) at such a rate that the reaction mixture spontaneously refluxed. The mixture was refluxed for a further 20 min, then cooled, and 10% sulphuric acid (100 ml) and ice were added. The organic layer was separated, washed several times with 5% sulphuric acid, then with sodium hydrogen carbonate, and finally with water. The organic layer was dried ($MgSO_4$) and evaporated at reduced pressure. The aqueous washings were extracted with ether, and the ether layer was dried and evaporated. The residue was combined with that from the organic layer above and distilled at 100° and 3 mmHg to give the hydroxy-ester (8), $\nu_{max.}$ 3500m, 2960s, and 1730s cm^{-1}. To a refluxing solution of 85% hydrazine hydrate (30 ml) and ethanol (10 ml), the alcohol (8) was added in 1·5 h with stirring. The mixture was refluxed for a further 15 min and then slowly cooled to give *crystals* of (9), m.p. 164—165° [12 g, 40% from (1)] (Found: C, 58·9; H, 8·7; N, 15·5. $C_9H_{16}N_2O_2$ requires C, 58·7; H, 8·7; N, 15·2%), $\nu_{max.}$ (hexachlorobutadiene mull) 3380, 3300, 3200, 2940, and 1740 cm^{-1}.

Spiro[*norbornane*-2,5′-*oxazolidin*]-2′-*one* (10).—To a cooled (0°) suspension of (9) (10 g) in a mixture of water (100 ml), glacial acetic acid (34 ml), and ethanol-free ether (150 ml) was added a solution of sodium nitrite (4·15 g) in water (30 ml) at such a rate that the temperature never exceeded 4°. The solution was rapidly filtered through cotton wool into a cold flask, and the ethereal layer was separated and dried ($MgSO_4$). The aqueous layer was extracted with ether and the combined ether layers were filtered under N_2. Dried benzene (15 ml) was added to the filtrate, from which the ether was slowly distilled off and then, on a steam-bath, 7·5 ml of benzene was also distilled off. The solution was then cooled and concentrated at reduced pressure to give crystals which were filtered off and triturated with n-pentane to leave the *spiro-compound* (10), m.p. 140° (6 g, 75%) (Found: C, 64·6; H, 7·7; N, 8·1. $C_9H_{13}NO_2$ requires C, 64·6; H, 7·8 N, 8·4%), δ ($CDCl_3$) 6·35br (1H, exch. with D_2O), 3·4 (2H, s), and 2·4—1 (10H), $\nu_{max.}$ (hexachlorobutadiene mull) 3220, 2950, 2860, and 1760 cm^{-1}. Recrystallisation from benzene gave material of m.p. 94—95° with an i.r. spectrum identical with that of the compound of m.p. 140°.

exo-2-*Aminomethylbicyclo*[2.2.1]*heptan*-2-*ol* (4; n = 1).—To a 5M solution of sodium ethoxide in ethanol was added (10) (0·80 g dissolved in the minimum volume of ethanol). The mixture was refluxed for 2 h, the solvent was evaporated off, and water was added. Chloroform extracts of the water mixture were distilled at 80° and 1 mmHg to give the *amino-alcohol* (4; n = 1) (0·33 g, 40%) (Found: C, 68·4; H, 10·6; N, 10·0. $C_8H_{15}NO$ requires C, 68·5; H, 10·7; N, 9·9%), δ ($CDCl_3$) 2·66 (ABq), 2·4 (3H, s, exch. with D_2O), and 2·4—0·9 (10H).

Mixture of exo- (2; n = 2) *and* endo-2-*Cyanobicyclo*-[3.2.1]*octan*-2-*yl Acetate* (3; n = 2).—The preparation was carried out starting with bicyclo[3.2.1]octan-2-one [2a] (11 g, 0·089 mol) following the method for the preparation of (2) and (3) (n = 1) above. A *ca.* 65 : 35 mixture of (3) and (2) (n = 2) was distilled at 115—116° and 0·5 mmHg (13·8 g, 81%) (Found: C, 68·3; H, 7·9; N, 7·4. Calc. for $C_{11}H_{15}NO_2$: C, 68·4; H, 7·8; N, 7·3%).

exo- (6; n = 2) *and* endo-2-p-*nitrobenzamidomethylbicyclo*[3.2.1]*octan*-2-*ol* (7; n = 2).—The foregoing mixture of (2) and (3) (n = 2) (13·5 g) was treated with $LiAlH_4$ according to the procedure above for (2) and (3) (n = 1) to give a crystalline *ca.* 65 : 35 (see text) mixture of (4) and (5) (n = 2), b.p. 80° at 0·7 mmHg (5·9 g). This was

[15] V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, 1953, **18**, 1190.

[16] H. E. Carter, R. L. Frank, and H. W. Johnston, *J. Amer. Chem. Soc.*, 1952, **74**, 3818.

treated with 1 equiv. of *p*-nitrobenzyl chloroformate and pyridine in dried dioxan (use of carefully dried materials is essential to avoid hydrolysis to *p*-nitrobenzyl alcohol which is difficult to separate), according to the previous procedure for (6) and (7) ($n = 1$), to get 11 g of crystalline material. A sample (9 g) of this material was purified by p.l.c. on silica gel (eluant chloroform–methanol 9 : 1, R_F 0·6). Fractional crystallisation from benzene gave crystals (0·25 g), m.p. 152—154°, as the less soluble fraction (Found: C, 61·1; H, 6·6; N, 8·5. Calc. for $C_{17}H_{22}N_2O_5$: C, 61·1; H, 6·7; N, 8·4%), δ (C_6D_6) 7·82, 7·74, 6·87, and 6·79 (4H, AB system), 5·1br (1H, rapidly exchanges with water), 4·8 (2H, s), 3·23 (2H, eight signals, which on shaking with D_2O slowly changes into a typical ABq centred at 3·23), and 2—1 (13H). The mother liquor, after several other fractional recrystallisations gave crystals (0·8 g), m.p. 98—100°, as the more soluble fraction (Found: C, 61·1; H, 6·7; N, 8·5%), δ (C_6D_6) as above for the isomer of m.p. 152—154° but in place of the system of eight signals there was a doublet centred at 3·16 (J 7 Hz).

Deamination of (4) *and* (5) ($n = 1$ *or* 2).—Compounds (6) and (7) ($n = 2$) were hydrogenolysed as described above for (6) and (7) ($n = 1$). Deaminations were carried out as in the following example. To an ice-cooled solution of the hydrochloride of (4; $n = 2$) in water (2 ml), from the hydrogenolysis of (6; $n = 2$) (0·05 g), was added glacial acetic acid (0·18 ml) and then, within 1 h with stirring, 40% aqueous sodium nitrite (0·5 ml). The mixture was maintained at 0° for 6 h and then at room temperature for a further 6 h, and then repeatedly extracted with ether. The ether layer was evaporated, bicyclo[3.2.1]octan-3-one was added as an internal standard, and the mixture was chromatographed on a 6 ft × 1/8 in 15% polypropylene glycol on Chromosorb W 80—100 mesh column.

Reactions of Bicyclo[2.2.1]*heptan-2-one and Bicyclo*[3.2.1]*octan-2-one with Diazomethane.*—The reactions were carried out as in the following example. To a solution of norbornan-2-one (0·033 g) in methanol (3 ml) was added diazomethane in ether (0·25 ml; 0·75M). After the yellow colour had disappeared, the mixture was chromatographed on a column identical with that used in the deaminations above (column temp. 122°, N_2 flow 20 ml min^{-1}; retention times : norbornan-2-one 12 min, bicyclo[3.2.1]octan-3-one 15 min, bicyclo[3.2.1]octan-2-one 19 min).

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