Synthesis of 2-Substituted Bicyclo[2.1.0]pentanes from Bicyclo[3.1.0]hexan-2-one

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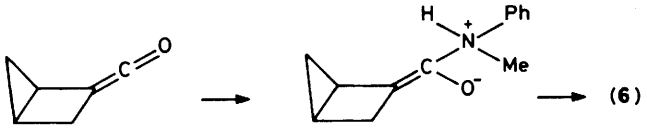
Bicyclo[3.1.0]hexan-2-one (**1**) was converted into the 3-diazo derivative (**4**), which was ring-contracted thermally to give a variety of amides and esters of bicyclo[2.1.0]pentane-2-carboxylic acid as *exo*- and *endo*-stereoisomers. Conversion of the acids into the corresponding methyl ketones and then Baeyer–Villiger reaction has led to *endo*- and *exo*-bicyclo[2.1.0]pentan-2-yl acetates which differed markedly in solvolytic reactivity.

Formation of cyclopropyl carbinyl cations within a relatively rigid molecular framework has provided some insight into the stereoelectronic requirements and the nature of the very effective stabilisation of the cation provided by the cyclopropyl group.[1] In an extension of our work on the solvolysis or deamination of 2-substituted bicyclo[3.1.0]hexyl derivatives,[2] we required a route to 2-substituted bicyclo[2.1.0]pentyl compounds as precursors of the corresponding 2-cation. During our development of such a route, however, the solvolysis of bicyclo[2.1.0]pentan-2-yl 3,5-dinitrobenzoates was reported by Wiberg's group,[3] and this led us to abandon any solvolysis studies. As our synthesis of bicyclo[2.1.0]pentan-2-yl derivatives was different from that chosen by Wiberg, however, we report our synthetic work here.[4]

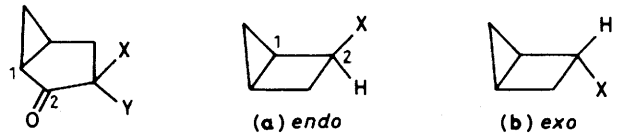
Base-catalysed condensation of bicyclo[3.1.0]hexan-2-one (**1**) with ethyl formate gave the 3-hydroxymethylene compound (**2**) in 74% yield. This with diethylamine gave the corresponding enamine (**3**); this was not fully characterised but had an n.m.r. spectrum in full accord with the given structure. The enamine, treated with tosyl azide after the method of Yates and co-workers,[5] gave 3-diazobicyclo[3.1.0]hexan-2-one (**4**) in 55% yield based on starting ketone (**1**) consumed. The yield of diazo ketone was not improved by use of methanesulphonyl azide in place of tosyl azide.

Thermal Wolff rearrangement of diazo ketone (**4**) in boiling *N*-methylaniline yielded the expected *N*-methylbicyclo[2.1.0]-pentane-2-carbanilide as a mixture of *endo* and *exo* epimers (**6a** and **b**) with an n.m.r. spectrum containing a cyclopropylmethylene signal, but no olefinic signal; this indicated that no ring-opening of the strained bicyclic system had occurred. The spectrum showed two *N*-methyl peaks at δ 3.23 and 3.29 in the ratio 80:20. These peaks were assigned to the 2-*endo*-epimer (**6a**) and the 2-*exo*-epimer (**6b**) respectively on the basis that the *endo*-*N*-methyl group would be shielded by the face of the cyclopropyl ring[6] and appear at higher field than the corresponding signal for the *exo* derivative. On mechanistic grounds the *endo*-epimer was expected to be the major product. After attack of *N*-methylaniline on the intermediate ketene, protonation of the formed enol would be easier from the less hindered *exo*-face (Scheme, only one geometric isomer shown).



Scheme.

Kinetic control in the production of this 80:20 ratio of epimers was shown when a boiling solution of potassium t-butoxide in t-butyl alcohol established an equilibrium *endo*:*exo* ratio of *ca.* 50:50, presumably *via* the 2-carbanion.



(a) *endo* (b) *exo*

(**1**) X = Y = H
(**2**) XY = =CHOH
(**3**) XY = =CHNEt$_2$
(**4**) XY = =N$_2$
(**5**) X,Y = H, O[CH$_2$]$_2$OH

(**6**) X = CON(Me)Ph
(**7**) X = CONHPh
(**8**) X = CO$_2$[CH$_2$]$_2$OH
(**9**) X = CO$_2$H
(**10**) X = CO$_2$Me
(**11**) X = NHCO$_2$Me
(**12**) X = Ac
(**13**) X = OAc
(**14**) X = OH
(**15**) X = CH$_2\overset{+}{N}$PhMe$_2$ I$^-$

Initially we observed a rapid equilibration between the *N*-methylanilides (**6a**) and (**6b**) to a 50:50 ratio when they were heated in a sealed glass tube *in vacuo* at 200 °C, a reaction we assumed[4] had proceeded *via* the Cheswick mechanism[7] which involved breaking of the 1,4-bond and a 'ring flip' of the C-5 methylene in the diradical, followed by reclosure. It was later shown, however, that the reaction was dependent on the type of glass used. In 'Pyrex' tubes little reaction was observed at 230 °C after 0.5 h, but on heating to 235 °C for 4 h about 90% ring-opening to a mixture of *N*-methylcyclopentene-1- and -3-carbanilide had occurred (olefinic signals in n.m.r. spectrum). We conclude that our so-called 'thermal equilibration' was in fact a base-catalysed reaction caused by alkali in the glass tube originally used, and we withdraw our earlier report.[4] The ring-opening of the bicyclopentane (**6**) to cyclopentenes at 235 °C, presumably *via* a [1,2]-shift of 5-H in the diradical, occurs at a lower temperature than that reported for the simple bicyclopentanes[8] (330 °C).

Chemical evidence for the bicyclo[2.1.0]pentane skeleton in anilide (**6**) was observed when catalytic hydrogenation with palladium–charcoal cleaved the C-1, C-4 bond to yield *N*-methylcyclopentanecarbanilide, identical with that formed from 2-diazocyclohexanone in boiling *N*-methylaniline. Attempts to separate the *endo*-and *exo*-*N*-methylanilide (**6a** and **b**) failed, but the corresponding anilides (**7**) formed from diazo ketone (**4**) in boiling aniline were separated and fully characterised. The n.m.r. spectra of the epimers showed that the chemical shift of the 2-H could be used for stereochemical assignments. When 2-H was *exo* to the bicyclic system as in *endo*-anilide (**7a**) its signal appeared at δ 3.2, whilst in the *exo*-anilide (**7b**) 2-H was shielded by the cyclopropane ring and appeared at δ *ca.* 2.7, overlapping other signals. This shielding of 2-*endo*-protons relative to 2-*exo*-protons was observed in other 2-substituted

derivatives and is a general phenomenon, noted also by Wiberg's group.[9]

Hydrolysis of the anilides to simple carboxylic acids required forcing conditions and, in particular, acid hydrolysis led to ring-opening of the bicyclopentane ring-system and formation of the cyclopentene-1- and -3-carbanilide among other products. Attention was therefore turned to the preparation of bicyclo-[2.1.0]pentanecarboxylic esters, more suitable for further transformation.

Photochemical Wolff rearrangement[10] of the diazo ketone (**4**) in ether–methanol gave the epimeric methyl esters (**10**), but in a low yield of 20% due to their volatility. We therefore attempted the thermal rearrangement to esters in high boiling alcohols. After benzyl alcohol and 1-phenylethanol had proved unsatisfactory, boiling ethylene glycol proved particularly suitable as any excess could be removed by aqueous work-up. Early erratic results were eliminated by addition of pyridine or collidine to the glycol; this improvement was probably due to the nucleophilic properties of the amine, the intermediate ketene reacting to give an acylpyridinium salt prior to attack by the glycol. Use of sodium carbonate or silver oxide[11] as a base did not give the same reproducible results.

The epimeric 2-hydroxyethyl bicyclo[2.1.0]pentane-2-carboxylates (**8**) were hydrolysed to give 2-carboxylic acids (**9**) in 64% yield from the diazo ketone (**4**). A small amount of neutral 3-(2-hydroxyethoxy)bicyclo[3.1.0]hexan-2-one (**5**) was also recovered, this probably arising by protonation of the diazo ketone followed by nucleophilic attack of solvent.

The acids (**9**), in an *endo*:*exo* ratio of 60:40, were separated by preparative g.l.c. (p.l.c.) of their methyl esters. Each ester was found to epimerise in a boiling solution of sodium methoxide in methanol to the same equilibrium mixture of 57:43 *endo*- and *exo*-ester (**10a** and **b**) with no ring-opening. Basic hydrolysis of each ester at 20 °C in 0.3M-sodium hydroxide proceeded without epimerisation, however, so that the acids (**9a**) and (**9b**) were each available in a pure state.

Two standard routes from acids (**9**) to bicyclopentanes having a suitable leaving group at C-2 were investigated. In the first, the epimeric acids were converted into the 2-isocyanates *via* the Curtius rearrangement of the acid azides; these isocyanates were not isolated, but converted into the methyl bicyclo[2.1.0]pentan-2-ylcarbamates (**11**) and separated by g.l.c.

The *N*-nitrosation of carbamates and subsequent decomposition of the product in protic solvents under acidic or basic conditions has proved an excellent route to carbonium ions *via* the corresponding diazo alkanes, and this offered a route to the bicyclopentan-2-yl cation.[12] As a model reaction, methyl cyclobutylcarbamate, with dinitrogen tetraoxide in tetrachloromethane, gave greater than 90% *N*-nitroso derivative (as judged by n.m.r. spectrometry; a downfield shift of the OMe group being observed on nitrosation) although the product was not fully characterised.

When the method[12] was applied to the more sensitive bicyclopentylcarbamates (**11**), however, use of one equivalent of dinitrogen tetraoxide gave only 30% *N*-nitrosation (n.m.r.) and the product could not be purified. Excess of N_2O_4 led to unidentified water-soluble products due possibly to attack of the reagent on the weak C-1, C-4 bond. Because of these difficulties the route was abandoned.

A second, more successful route to the 2-alcohols (**14**) involved the conversion of each bicyclopentanecarboxylic acid (**9**) into the corresponding methyl ketone (**12**) using methyllithium at low temperature and conversion of the ketones into the acetates (**13**) by the Baeyer–Villiger reaction.[13] Surprising differences were noted between the *exo*- and *endo*-series, however. Both methyl ketones were less reactive than acetylcyclopentane towards 3-chloroperbenzoic acid. Such lack of reactivity is probably due to ring strain, which results in a greater than normal percentage of *s*-character in the orbital of C-2 containing the migrating electron pair. Acetylcyclopropane, where a similar effect is present, gives a satisfactory Baeyer–Villiger rearrangement only with the powerful trifluoroperacetic acid (TFA).[14] However, reaction of TFA with the epimeric acetylbicyclopentanes (**12**) gave a complex mixture which, from the i.r. spectrum, contained trifluoroacetates, and after p.l.c. only a low yield of *exo*-acetate (**13b**) was obtained. TFA, even with buffer present, was clearly too acidic for the bicyclic system. After further investigation, *endo*-acetyl compound (**12a**) was found to rearrange with 3-chloroperbenzoic acid in boiling chloroform containing potassium carbonate: conditions which left the *exo*-acetyl compound (**12b**) unaffected. The latter ketone rearranged with monopermaleic acid, a reagent where the free carboxy group may provide an internal proton source to promote rearrangement.[15] This acidic reagent gave polymeric material when used on the *endo*-acetyl compound (**12a**), where the expected product (**13a**) would be expected to be readily decomposed to the 2-cation by acid (see below).

The greater reactivity of the *endo*-acetyl compound (**12a**) relative to the *exo*-derivative (**12b**) in the Baeyer-Villiger rearrangement is noteworthy. The most electron-rich alkyl group normally migrates[13] and only in the *endo*-series is the bent C-1,C-4 bond set up to provide electron density at the rear of the C-2 orbital involved in the carbon-to-oxygen migration.

Wiberg has shown[3] that in solvolysis the *endo*-bicyclo-[2.1.0]pentyl 3,5-dinitrobenzoate reacts 10^7 times faster than the corresponding *exo*-3,5-dinitrobenzoate due to this type of interaction of the C-1,C-4 bond with the developing cation at C-2 in the *endo*-series.

This differing reactivity was also reflected in the behaviour of the 2-acetoxy derivatives upon hydrolysis. The *exo*-acetate (**13b**) hydrolysed normally with sodium hydroxide to give *exo*-bicyclo[2.1.0]pentan-2-ol (**14b**), characterised as the 4-nitrobenzoate ester, m.p. 81.5—83 °C. The more labile *endo*-acetate (**13a**), containing 5% of 4-acetoxycyclopent-1-ene, when hydrolysed with 0.8M-sodium hydroxide at ambient temperature gave *endo*-bicyclo[2.1.0]pentan-2-ol (**14a**) containing 25% more cyclopent-3-enol than expected (~30%), showing that the solvolysis of the acetoxy group in the *endo*-series was competing with hydrolysis of the acetate. A purer product was obtained by reduction of the *endo*-acetate with lithium aluminium hydride, but attempts to form a crystalline 4-nitrobenzoate ester using standard methods failed.

Experimental

M.p.s were determined with a Kofler block hot-stage apparatus and are uncorrected. I.r. spectra were obtained on a Perkin Elmer 125 or Unicam SP 1000 instrument. N.m.r. spectra were obtained on Varian A 60A or Perkin Elmer R 32 spectrometers. Mass spectra were recorded on an A.E.I. MS 902 instrument. G.l.c. analyses were carried out on a Perkin Elmer F.11 using 150 ft and 200 ft glass or stainless steel capillary columns. Preparative separations were performed on either the Varian Aerograph A700 or 1527B machines. Kieselgel GF 254 (Merck) was used for t.l.c. Solutions in organic solvents were dried over sodium sulphate unless otherwise stated.

3-*Hydroxymethylenebicyclo*[3.1.0]*hexan-2-one* (**2**).—Bicyclo-[3.1.0]hexan-2-one (**1**)[16] (12.5 g), ethyl formate (14.3 g, distilled from P_2O_5), and sodium hydride (50% dispersion in mineral oil; 14.5 g) were added to dry ether (300 ml), and the mixture was stirred whilst ethanol (0.3 ml) was added, the whole being cooled by a water-bath. After 18 h, water (30 ml) was carefully added followed by aqueous potassium hydroxide (2M; 50 ml). The aqueous layer was separated, and the ether was washed with aqueous potassium hydroxide (M; 2 × 100 ml). The

combined aqueous extracts were acidified (pH 3) with conc. hydrochloric acid and extracted with ether (3 × 150 ml) to give the *hydroxymethylene derivative* (**2**) which was distilled, b.p. 113—117 °C/13 mmHg, to give a solid, m.p. 62—64 °C (11.9 g, 74%) (Found: C, 67.8; H, 6.3. $C_7H_8O_2$ requires C, 67.7; H, 6.5%); $\nu_{max.}$ 2 650v br (OH), 1 680 (C=O), and 1 612 cm^{-1}; $\lambda_{max.}$ 266 nm (ε 7 320).

3-*Diazobicyclo*[3.1.0]*hexan*-2-*one* (**4**).—3-Hydroxymethylenebicyclo[3.1.0]hexan-2-one (**2**) (8.5 g, 0.067 mol) was heated to its m.p., and diethylamine (7.3 g, 0.10 mol) was added. After 1 h, excess of amine and water were removed under reduced pressure to yield the crude enamine (**3**) (12.3 g) [$\nu_{max.}$ 1 670 (C=O) and 1 575 cm^{-1} (C=O); δ 0.45 (1 H, q, cyclopropyl), 0.9—1.3 (1 H, m, cyclopropyl), 1.2 (6 H, t, 2 × CH_3CH_2), 1.8 (2 H, m, 1- and 5-H), 2.85 (2 H, s, allylic CH_2), 3.3 (4 H, q, 2 × CH_3CH_2), and 7.17 (1 H, t, olefinic H)]. A solution of the enamine (**3**) in ether (15 ml) was stirred with toluene-*p*-sulphonyl azide (14.0 g, 0.071 mol), and the reaction was followed by i.r. spectrometry (azide 2 112, diazo ketone 2 082 cm^{-1}). After 40 h sodium hydroxide (2 M; 40 ml) was added to hydrolyse the unchanged azide, and after a further 1 h the mixture was extracted to give a total volume of ether of 150 ml. The ether was dried and cooled to −40 °C, when *N*,*N*-diethyl-*N'*-(*p*-tolylsulphonyl)formamidine[5] crystallised out and was filtered off (10.0 g), m.p. 77—78 °C. The filtrates on distillation (oil-bath temperature < 110 °C) gave the *diazo ketone* (**4**) (6.2 g, 74%) as a yellow oil, b.p. 69—72 °C/2 × 10^{-2} mmHg (Found: C, 58.9; H, 4.75; N, 22.8. $C_6H_6N_2O$ requires C, 59.0; H, 4.9; N, 22.9%); $\nu_{max.}$ 2 082 and 1 675 cm^{-1}; $\lambda_{max.}$ 248 (6 450) and 297 nm (4 900); δ 0.65 (1 H, m, cyclopropyl), 1.2 (1 H, m, cyclopropyl), 1.72 (2 H, m, 1- and 5-H), and 3.1 (2 H, m, CH_2). Use of methanesulphonyl azide in place of toluene-*p*-sulphonyl azide gave 20% diazo ketone after 2 h reaction time.

N-*Methylbicyclo*[2.1.0]*pentane*-2-exo- *and* -2-endo-*carbanilide* (**6**).—A solution of the diazobicyclohexanone (**4**) (2.1 g, 0.01 mol) in *N*-methylaniline (2 ml) was added dropwise to boiling *N*-methylaniline during 10 min. After a further 5 min the mixture was cooled, diluted with ether (50 ml), and washed successively with hydrochloric acid and aqueous sodium hydrogen carbonate. The ring-contracted anilides were distilled after removal of ether, b.p. 158 °C (air-bath)/7 mmHg, to give a viscous oil, further purified by rapid chromatography on 'Florisil' with benzene–ether as eluant to remove fast running coloured impurities (2.2 g, 64%) (Found: C, 77.15; H, 7.3; N, 7.6. $C_{13}H_{15}NO$ requires C, 77.6; H, 7.5; N, 7.0%); $\nu_{max.}$ 1 660 cm^{-1}; δ 0.4—0.95 (2 H, m, cyclopropyl CH_2), 1.0—3.2 (5 H, m, ring CH and CH_2), 3.23 and 3.29 (3 H, 2 × s, ratio 80:20, *N*-Me of *endo*- and *exo*-anilide), and 7.0—7.7 (5 H, m, Ph). The epimers were not separated by either g.l.c. or chromatography. When the epimers were heated in an evacuated sealed Carius tube (non-'Pyrex') at 225 °C for 0.5 h the ratio of *endo*:*exo* epimers changed to 53:47. A similar ratio was observed when the anilides were heated in Bu^{t}OH–Bu^{t}OK for 1 h. In a 'Pyrex' tube the epimer ratio was unaffected at 225 °C, but at 235 °C for 4 h 90% ring-opening to *N*-methylcyclopentene-1- and -3-carbanilide was found.

Bicyclo[2.1.0]*pentane*-2-*carbanilides* (**7**).—The bicyclic diazo ketone (**4**) (4.7) g, 0.38 mol) reacted with boiling aniline in the same way as for *N*-methylaniline described above, and the epimeric anilides were separated by column chromatography on 'Florisil'. The exo-*anilide* (**7b**) (0.8 g, 11%) had m.p. 188—188.5 °C (from chloroform) (Found: C, 76.8; H, 6.8; N, 7.8. $C_{12}H_{13}NO$ requires C, 77.0; H, 7.0; N, 7.5%); $\nu_{max.}$(KCl) 1 660 cm^{-1}; δ 0.8 (2 H, m, cyclopropyl CH_2), 1.8 (3 H, complex m, 1- and 4-H, and 3-H_{endo}), 2.5 (2 H, m, 2-H_{endo} and 3-H_{exo}), and 7.3 (6 H, m, Ph and NH).

The endo-*anilide* (**7a**) had m.p. 120—121 °C (from benzene) (2.7 g, 38%) (Found: C, 76.9; H, 7.0; N, 7.75%); $\nu_{max.}$(KCl) 1 660 cm^{-1}; δ 0.8 (2 H, m, cyclopropyl CH_2), 1.8 (3 H, m, 1- and 4-H, and 3-H_{endo}), 2.5 (1 H, tt, 3-H_{exo}), 3.2 (1 H, m, 2-H_{exo}), and 7.3 (6 H, m, Ph and NH).

N-*Methylcyclopentanecarbanilide*.—(*a*) 2-Diazocyclohexanone (1.0 g) was dropped into an excess of boiling *N*-methylaniline and, after work-up in the usual way, gave *N*-methylcyclopentanecarbanilide,[5] b.p. 115 °C (air-bath)/0.5 mmHg (1.1 g, 70%), m.p. 33—35 °C from light petroleum (b.p. 60—80 °C)–ether.

(*b*) The mixture of *endo*- and *exo*-*N*-methylbicyclopentane-2-carbanilide (0.095 g) in ethanol was hydrogenated with 10% Pd–C until uptake of hydrogen was 98% of the theoretical. Work-up gave the monocyclic *N*-methylanilide (0.09 g, 95%), m.p. 32 °C, identical in all respects with the sample prepared in (*a*).

Acid-catalysed Ring-opening of N-*Methylbicyclo*[2.1.0]*pentane*-2-*carbanilides*.*—A mixture of *N*-methyl *endo*-and *exo*-carbanilide (0.5 g; ratio 80:20) in methanol (25 ml) and hydrochloric acid (2M; 25 ml) was heated on a steam-bath for 20 min. Extraction with ether and washing of the extract with water gave a complex mixture (t.l.c.) of crude ring-opened amides (0.38 g) which were chromatographed on 'Kieselgel G' with benzene–ether as eluant. First eluted was N-*methylcyclopent*-1-*enecarbanilide* as a gum, purified by bulb-to-bulb distillation (Found: M^+, 201.1144. $C_{13}H_{15}NO$ requires *M*, 201.1154); $\nu_{max.}$($CHCl_3$) 1 640 cm^{-1} (C=O); δ 7.5—7.1 (5 H, m, Ph), 5.58 (1 H, br s, olefinic H), 3.30 (3 H, s, NMe), and 3.2—1.6 (6 H, m, ring CH_2). Next, after some mixed fractions, N-*methylcyclopent*-2-*enecarbanilide* was eluted and purified as above (Found: M^+ 201.1146); $\nu_{max.}$ 1 640 cm^{-1} (C=O); δ 7.6—7.1 (5 H, m, Ph), 5.85 (1 H, m, olefinic H), 5.55 (1 H, m, olefinic H), 3.50 (1 H, m, CHCO), 3.30 (3 H, s, NMe), and 2.6—1.6 (4 H, m, ring CH_2).

Further elution gave only mixed fractions whose n.m.r. spectra showed varying olefinic and *N*-methyl signals among others.

2-*Hydroxyethyl Bicyclo*[2.1.0]*pentane*-2-endo- *and* -2-exo *carboxylate* (**8**).—3-Diazobicyclo[3.1.0]hexan-2-one (**4**) (1.0 g) was added dropwise to a mixture of ethylene glycol (7 ml) and collidine (1.5 ml) at 180 ± 5 °C. After each drop nitrogen was evolved and the yellow colour disappeared after a few seconds. After the addition the mixture was maintained at 180 °C for 2 min and was then cooled. Four such reaction mixtures were combined and poured into brine (80 ml), and were extracted with chloroform (4 × 40 ml). After removal of the chloroform the residue was taken up in ether (100 ml) and the extract was washed with 2M-hydrochloric acid to remove collidine, and then with brine (10 ml). The total washings were re-extracted with ether (4 × 30 ml). The combined ether extracts, after being dried, gave the crude 2-hydroxyethyl ester (**8**) as a dark oil (3.8 g). An analytical sample prepared by p.l.c. [15% Carbowax (10 ft) at 172 °C] (Found: C, 60.6; H, 7.55. $C_8H_{12}O_3$ requires C, 61.5; H, 7.7%) showed $\nu_{max.}$ 3 500 and 1 723 cm^{-1} and the expected n.m.r. spectrum for a mixture of 2-epimers.

endo-*and*exo-*Bicyclo*[2.1.0]*pentane*-2-*carboxylic Acids* (**9**).—The crude 2-hydroxyethyl esters (3.7 g) were stirred in aqueous sodium hydroxide (2M; 40 ml) at 55 °C for 3 h. Extraction (ether) of the alkaline solution and work-up gave a small quantity of

* This experiment was performed by Dr. D. E. Kitson.

3-(2-hydroxyethoxy)bicyclo[3.1.0]hexan-2-one (**5**), characterised as a 2,4-*dinitrophenylhydrazone*, m.p. 146—148 °C from chloroform–light petroleum (b.p. 60—80 °C) (Found: C, 50.05; H, 5.0; N. 16.5. $C_{14}H_{16}N_4O_6$ requires C, 50.0; H, 4.8; N, 16.7%). Acidification of the aqueous layer (pH 3) and extraction with ether (4 × 40 ml) gave the crude *exo*- and *endo*-carboxylic acids (**9**) (2.5 g, 64%); $\nu_{max.}$ 3 600—2 400, and 1 705 cm^{-1}. The acids yielded a 4-*bromophenacyl ester* (unknown stereochemistry), m.p. 67—67.5 °C (Found: C, 54.35; H, 4.45; Br, 26.4. $C_{14}H_{13}BrO_3$ requires C, 54.5; H, 4.2; Br, 25.9%). Conversion into the methyl esters (**10**) with diazomethane and g.l.c. analysis indicated an *exo*:*endo* ratio of 40:60 ± 1%. P.l.c. (20 ft; 30% Carbowax 20M; 139 °C) then gave the exo-*methyl ester* (Found: C, 66.85; H, 8.1. $C_7H_{10}O_2$ requires C, 66.7; H, 7.9%), $\nu_{max.}$ 1 740 cm^{-1}; δ 0.7 (2 H, m, cyclopropyl CH_2), 1.7 (3 H, m, 1- and 4-H, and 3-H_{endo}), 2.38 (2 H, m, 2-H and 3-H_{exo}), and 3.67 (3 H, s, OMe); followed by the endo-*methyl ester* (Found: C, 66.35; H, 8.05%), $\nu_{max.}$ 1 740 cm^{-1}; δ 0.7 (2 H, m, cyclopropyl CH_2), 1.6 (3 H, m, 1- and 4-H, and 3-H_{endo}), 2.3 (1 H, td, 3-H_{exo}), 3.2 (1 H, dt, 2-H_{exo}), and 3.57 (3 H, s, OMe).

The epimeric methyl esters were also formed in an *exo*:*endo* ratio of 40:60 by irradiation of 3-diazobicyclo[3.1.0]hexan-2-one (**4**) (1.9 g) in ether (1 l) containing methanol (15 ml) in an Hanovia irradiation apparatus for 90 h. Fractional distillation yielded the epimeric mixture (0.4 g, 20%), b.p. 155—160 °C.

The pure *exo*- and *endo*-bicyclo[2.1.0]pentane-2-carboxylic acids were obtained by basic hydrolysis of the appropriate methyl ester with sodium hydroxide (0.3M) at 20 °C for 40 h followed by acidification. Both acids showed $\nu_{max.}$ 3 500—2 500, and 1 705 cm^{-1}, and each acid gave an n.m.r. spectrum closely resembling that of the corresponding methyl ester, but with a low-field signal (OH) replacing the OMe signal.

Methyl Bicyclo[2.1.0]*pentan-2-ylcarbamates* (**11**).—A 40:60 mixture of the epimeric bicyclopentanecarboxylic acids (**10**) (0.9 g, 0.008 mol) was converted into the acid chlorides by means of oxalyl chloride (1.9 g, 0.015 mol) in benzene (2 ml) with one drop of dimethylformamide at 0 °C. After 1 h, excess of reagent was removed under reduced pressure at 40 °C and the residue was taken up in dry acetone (2 ml) and added dropwise to a stirred solution of sodium azide (1.0 g, 0.015 mol) in water (5 ml) at 0 °C. After 5 min, extraction with chloroform (2 × 10 ml) yielded a solution of the crude azides, which was dried over anhydrous calcium sulphate ($\nu_{max.}$ 2 160 and 1 710 cm^{-1}). After addition of dry methanol the total volume was reduced to 5 ml, a further quantity of dry methanol (2 ml) was added and the solution was heated under reflux for 16 h. The crude mixture of carbamates obtained on removal of solvent showed (by n.m.r. spectrometry) two OMe singlets at δ 3.57 and 3.61 in the ratio of 60:40, corresponding to *endo* and *exo* epimers. These were separated by g.l.c. (10 ft; Carbowax 20M; temperature programming 150—140 °C) to give the exo-*carbamate* (**11b**) (0.16 g, 14%), m.p. 55—57 °C (Found: C, 59.5; H, 7.7; N, 9.7. $C_7H_{11}NO_2$ requires C, 59.5; H, 7.8; N, 9.9%); $\nu_{max.}$(KCl) 3 340 and 1 700 cm^{-1}; δ 0.7 (2 H, m, cyclopropyl CH_2), 1.7 (4 H, m, 3-H_2, and 1- and 4-H), 3.5 (1 H, m, 2-H), 3.61 (3 H, s, OMe), and 5.8 (1 H, br s, NH); and the endo-*carbamate* (**11a**) (0.32 g, 28%), m.p. 34—36 °C (Found: C, 59.35; H, 7.7; N, 9.55%); $\nu_{max.}$(KCl) 3 300 and 1 705 cm^{-1}; δ 0.7 (2 H, m, cyclopropyl CH_2), 1.3 (1 H, m, 3-H_{endo}), 2.5 (1 H, tdd, 3-H_{exo}), 3.57 (3 H, s, OMe), 4.2 (1 H, m, 2-H), and 5.4 (1 H, br s, NH).

Treatment of the mixture of carbamates with 90% of the theoretical amount of dinitrogen tetraoxide in tetrachloromethane with solid sodium hydrogen carbonate at −20 °C for 30 min showed 30% *N*-nitrosation as evidenced in the n.m.r. spectrum by the drop in intensity of the OMe signals at δ 3.5—3.7 and the appearance of two new peaks at δ 4.0 and 4.1. The intensity of the cyclopropyl CH_2 signal showed that the bicyclic system was stable under these conditions.

Treatment of the epimeric bicyclopentyl acid chlorides with *p*-bromoaniline yielded the *p*-bromoanilides, separable by chromatography on 'Kieselegel' Merck with 10% ether–benzene as eluant. The exo-(p-*bromoanilide*) had m.p. 173 °C [from light petroleum (b.p. 60—80 °C)–ether–benzene] (Found: C, 54.0; H, 4.35; N, 5.5; Br, 30.6. $C_{12}H_{12}BrNO$ requires C, 54.2; H, 4.5; N, 5.3; Br, 30.1%). The endo-(p-bromoanilide) had m.p. 132 °C (from benzene) (Found: C, 54.05; H, 4.4; N, 5.3; Br, 30.5).

exo-2-*Acetylbicyclo*[2.1.0]*pentane* (**12b**).—A solution of the 2-*exo*-bicyclopentane acid (1.1 g, 0.01 mol) in dry ether at −40 °C was stirred whilst ethereal methyl-lithium (0.4M; 25 ml, 0.01 mol) was added dropwise under N_2 during 30 min. The solution was raised to −10 °C and further methyl-lithium (27 ml, 0.011 mol) was added to the vigorously stirred mixture during 1 h. After a further 30 min at −10 °C the mixture was cooled to −50 °C and rapidly added to ice–water (50 ml). Extraction with ether gave the crude *exo*-acetyl derivative, b.p. 135—145 °C (air-bath) (0.7 g, 64%). Acidification and extraction (ether) of the aqueous layer gave unchanged acid (0.22 g, 20% recovered). The *exo*-acetyl derivative had $\nu_{max.}$ 1 710 cm^{-1}; δ 0.7 (2 H, m, cyclopropyl CH_2), 1.7 (3 H, complex m, 1-and 4-H, and 3-H_{endo}), 2.10 (3 H, s, CH_3CO), 2.3 (1 H, m, 3-H_{exo}), and 2.6 (1 H, m, 2-H) (there was no evidence of dimethylcarbinol formation in the product). The *exo*-2-acetylbicyclopentane was characterised as the 2,4-*dinitrophenylhydrazone*, from light petroleum (b.p. 60—80 °C)–chloroform, m.p. 107 °C (Found: C, 53.7; H, 4.9; N, 19.6. $C_{13}H_{14}N_4O_4$ requires C, 53.8; H, 4.8; N, 19.3%).

endo-2-*Acetylbicyclo*[2.1.0]*pentane* (**12a**).—The *endo*-bicyclopentane acid (1.65 g, 0.015 mol), treated in the same manner as the *exo*-acid above, gave the *endo*-2-acetyl derivative (1.1 g, 67%) (together 15% of unchanged acid); $\nu_{max.}$ 1 710 cm^{-1}; δ 0.5 (2 H, m, cyclopropyl CH_2), 1.6—2.4 (4 H, m, 1- and 4-H, and 3-H_2), 2.02 (3 H, s, CH_3CO), and 3.2 (1 H, dt, 2-H). The 2,4-*dinitrophenylhydrazone* had m.p. 141 °C from light petroleum (b.p. 60—80 °C)–chloroform (Found: C, 53.95; H, 4.9; N, 19.5%).

Baeyer–Villiger Oxidations of 2-*Acetylbicyclo*[2.1.0]*pentanes* (**12**).—(*a*) A mixture of epimeric 2-acetylbicyclopentanes (**12a** and **b**) (0.01 g) and 3-chloroperbenzoic acid (0.1 g, 30% excess) in dichloromethane was kept for 60 h at 20 °C. Usual work-up showed 70% starting ketones, 20% cyclopent-3-enyl acetate,[17] and 10% of mixed bicyclic acetates.

Under the same conditions but for 40 h, acetylcyclopentane was converted completely into cyclopentyl acetate.

(*b*) Hydrogen peroxide (90%; 1.5 g, 0.04 mol) was added dropwise to stirred trifluoroacetic anhydride (10.6 g, 0.05 mol) at 0 °C during 15 min. When homogeneous, the mixture was taken up in dichloromethane and the solution was added dropwise during 15 min to a well stirred mixture of dry, finely divided disodium hydrogen phosphate (14.2 g, 0.10 mol), a mixture of epimeric 2-acetylbicyclopentanes (**12**) (1.6 g, 0.015 mol), and dichloromethane (16 ml). The reaction mixture was heated under reflux for 2 h, after which the suspension was filtered and washed with dichloromethane. The filtrate was washed with 2M-sodium carbonate (2 × 20 ml) and dried to give a crude product (1.2 g), b.p. 140—150 °C; $\nu_{max.}$ 1 780 (trifluoroacetate), 1 735 (acetate) and 1 710w cm^{-1} (acetyl derivative). G.l.c. analysis (225 ft.; didodecyl phthalate capillary column) showed 20% starting ketone, 35% bicyclic acetates, and four other compounds totalling *ca.* 45%.

(*c*) 2-*endo*-Acetylbicyclo[2.1.0]pentane (**12a**) (0.33 g, 0.003 mol) was heated under reflux in chloroform (10 ml) with 3-chloroperbenzoic acid (1.6 g, 0.006 mol) and powdered

potassium carbonate (1.1 g, 0.008 mol) for 12 min. After having cooled, the mixture was washed successively with water, dil. aqueous sodium metabisulphite, aqueous sodium carbonate, and water. Careful removal of solvent from the dry solution, and distillation of the residue (bulb-to-bulb), gave the crude acetate (0.5 g), b.p. 130—150 °C (air-bath); $\nu_{max.}$ 1 735 cm^{-1}; δ 0.8 (2 H, m, cyclopropyl CH_2), 1.1—1.7 (2 H, m, 1- and 4-H), 1.95 (3 H, s, CH_3CO), 2.0 (1 H, m, 3-H), 2.48 (1 H, tdd, 3-H), and 5.0 (1 H, dt, 2-H). Signals at δ 7.25 and 5.68 indicated chloroform and cyclopent-3-enyl acetate[17] as impurities. G.l.c. analysis (225 ft; glass capillary column coated with didodecyl phthalate; 77 °C) showed *endo*-bicyclo[2.1.0]pentan-2-yl acetate (**13a**), unchanged ketone, and cyclopent-3-enyl acetate[17] in the proportions 90:5:5.

Under the same conditions the 2-*exo*-acetylbicyclopentane (**12b**) remained unchanged (g.l.c. analysis).

(*d*) Finely crushed maleic anhydride (0.5 g, 0.005 mol) was added to a stirred mixture of hydrogen peroxide (90%; 0.15 g, 0.004 mol) in dichloromethane (2 ml) cooled in ice. The solution was warmed, a solution of 2-*exo*-acetylbicyclopentane (**12b**) (0.11 g, 0.001 mol) in dichloromethane (2 ml) was added, and the stirred mixture was heated under reflux for 1 h. The cooled solution was washed successively with aqueous sodium carbonate, dil. aqueous sodium hydrogen sulphite, aqueous sodium carbonate, and water, the dichloromethane phase was dried, and the solvent was removed through a fractionating column. The residue was distilled (bulb-to-bulb), b.p. 130—150 °C (air-bath). The crude ester (0.1 g) was slightly contaminated with solvent: g.l.c. analysis showed only *exo*-bicyclo[2.1.0]pentan-2-yl acetate (**13b**) and starting ketone in the ratio 90:10; $\nu_{max.}$ 1 730 (with small peak at 1 710 cm^{-1}).

The *endo*-2-acetyl derivative (**12a**) under the same conditions gave no acetate but high boiling (polymeric ?) material showing $\nu_{max.}$ 1 730 cm^{-1}.

endo- *and* exo-*Bicyclo*[2.1.0]*pentan-2-ol* (**14**).—(*a*) *endo*-Bicyclopentan-2-yl acetate (**13a**) (0.3 g) from Baeyer–Villiger oxidation (*c*) above, containing 5% 2-*endo*-acetylbicyclopentane (**12a**) and 5% cyclopent-3-enyl acetate, was stirred at ambient temperature for 15 h with sodium hydroxide (0.8M; 15 ml). The solution was extracted with ether (3 × 10 ml) and tetrachloromethane (1 ml) was added. Removal of the ether was through a 10 in Dufton column, last traces being removed with a further 1 ml of tetrachloromethane as chaser. The n.m.r. spectrum included signals at δ 0.7 (m, cyclopropyl CH_2), 2.4 (m, allylic CH_2 in cyclopent-3-enol),[18] 4.3 (m, combined C*H*OH), and 5.7 (m, olefinic CH of cyclopent-3-enol). Integration of peaks at δ 4.3 and 5.7 indicated that the ratio of cyclopentenol to bicyclopental was 33:67. The g.l.c. analysis showed a larger proportion of cyclopent-3-enol due to partial ring-opening of the bicyclic alcohol in the injection block.

(*b*) A solution of *endo*-bicyclo[2.1.0]pentan-2-yl acetate (**13a**) (0.2 g crude) containing 2-*endo*-acetylbicyclopentane (**12a**) (18%) and cyclopent-3-enyl acetate (7%) in ether (10 ml) was added to a suspension of lithium aluminium hydride (0.12 g, 0.003 mol) in ether (10 ml). The mixture, after being stirred for 20 min, was treated cautiously with water (0.1 ml), aqueous sodium hydroxide (15% w/v; 0.1 mol), and water (0.4 ml) in turn. The dry granular precipitate was filtered off, and the filtrate was worked up as in (*a*) to give the endo-*bicyclopentan-2-ol* in (**14a**) tetrachloromethane; $\nu_{max.}(CCl_4)$ 3 500 cm^{-1}; $\delta(CCl_4)$ 0.7 (2 H, m, cyclopropyl CH_2), 2.4 (1 H, m, 3-H_{exo}), 3.1 (1 H, s, OH), and 4.3 (1 H, m, C*H*OH). The spectrum showed a signal for the olefinic impurity of cyclopent-3-enol[18] at δ 5.7, corresponding to 8% contamination (Found: M^+, 84.057 40. C_5H_8O requires *M*, 84.057 51).

(*c*) *exo*-Bicyclo[2.1.0]pentan-2-yl acetate (**13b**) [0.1 g, from Baeyer-Villiger oxidation (*d*)] was stirred with sodium hydroxide (0.5M; 10 ml) for 16 h. Extraction with ether gave the crude alcohol from which the last traces of ether were removed by co-distillation with a little tetrachloromethane through a short Dufton column; $\nu_{max.}$ 3 500 cm^{-1}. The alcohol was characterised as a 4-*nitrobenzoate ester*, m.p. 81.5—83 °C, purified by chromatography on 'Kieselgel G' (Merck) with benzene–dichloromethane as eluant (Found: C, 62.2; H, 4.9; N, 6.15. $C_{12}H_{11}NO_4$ requires C, 61.8; H, 4.7; N, 6.0%); δ (*inter alia*) 0.7—1.0 (2 H, m, cyclopropyl CH_2), 1.7—2.2 (4 H, m, 1- and 4-H, and 3-H_2), and 5.7 (1 H, m, 2-H_{endo}).

Bicyclo[2.1.0]*pentan-2-ylmethyldimethylanilinium Iodide* (**15**). —A mixture of epimeric bicyclo[2.1.0]pentane-2-carbanilides (**7**) (3.2 g) in ether (150 ml) was heated under reflux with lithium aluminium hydride (1.3 g) for 15 h. Water (1.3 ml), aqueous sodium hydroxide (15% w/v; 1.3 ml), and water (4 ml) were added successively, dropwise, and after being stirred for 20 min the solution was filtered, the ether was removed under reduced pressure, and the crude remanent amine was distilled (bulb-to-bulb), b.p. 140—150 °C/10 mmHg (air-bath) (2.6 g); $\nu_{max.}$ 3 450 cm^{-1}. A solution of the crude amine (2.3 g) in ethanol (6 ml) was heated under reflux with iodomethane (5.0 g) and anhydrous potassium carbonate for 30 min. Removal of the ethanol and crystallisation of the residue from acetone–ethanol gave the *methiodide* (**15**), m.p. 177 °C (Found: C, 51.5; H, 6.05; N, 4.3. $C_{14}H_{20}IN$ requires C, 51.05; H, 6.1; N, 4.2%).

When the methiodide (0.5 g) was heated with finely ground sodium hydroxide under a stream of nitrogen, liquefaction occurred at *ca.* 180 °C (bath temperature) with evolution of gas, which was trapped over CCl_4 (1.5 ml) at 0 °C. The n.m.r. spectrum of the solution showed very weak signals at δ 0.8 corresponding to cyclopropylmethylene, but no olefinic proton signal could be detected.

References

1 H. B. Wiberg, B. A. Hess, and A. J. Aske, in 'Carbonium Ions,' eds. G. A. Olah and P. von R. Schleyer, Wiley Interscience, New York, 1972, Vol. III: 'Cyclopropylcarbinyl and Cyclobutyl Cations,' p. 1295.
2 A. S. Bloss, P. R. Brook, and R. M. Ellam, *J. Chem. Soc., Perkin Trans. 2*, 1973, 2165.
3 K. B. Wiberg, V. Z. Williams, and L. E. Friedrich, *J. Am. Chem. Soc.*, 1970, **92**, 564.
4 Preliminary communication, P. R. Brook and B. V. Brophy, *Tetrahedron Lett.*, 1969, 4187.
5 M. Rosenberger, P. Yates, J. B. Hendrickson, and W. Wolf, *Tetrahedron Lett.*, 1964, 2285.
6 K. Tori and K. Kitahanoki, *J. Am. Chem. Soc.*, 1965, **87**, 386.
7 J. P. Cheswick, *J. Am. Chem. Soc.*, 1962, **84**, 3250; M. L. Halberstat and J. P. Cheswick, *ibid.*, p. 2688.
8 R. Criegee and A. Rimmelin, *Chem. Ber.*, 1957, **90**, 414.
9 K. B. Wiberg and D. E. Barth, *J. Am. Chem. Soc.*, 1961, **91**, 5124.
10 H. Meier and K. P. Zeller, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 32; L. Horner and E. Spitschka, *Chem. Ber.*, 1952, **85**, 225.
11 F. Arndt and B. Eistert, *Ber. Dtsch. Chem. Ges. B.*, 1935, **68**, 200.
12 R. A. Moss and F. C. Schulman, *Tetrahedron*, 1968, **24**, 2881; E. H. White, *J. Am. Chem. Soc.*, 1955, **77**, 6008.
13 C. H. Hassall, *Org. React.*, 1957, **9**, 74.
14 W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, 1955, **77**, 2287.
15 R. W. White and W. D. Emmons, *Tetrahedron*, 1962, **17**, 31.
16 W. A. Nelson and G. A. Mortimore, *J. Org. Chem.*, 1957, **22**, 1146.
17 R. Steyn and H. Z. Sabee, *Tetrahedron*, 1969, **26**, 3595.
18 E. L. Allred, J. Sonnenberg, and S. Winstein, *J. Org. Chem.*, 1960, **25**, 26.

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