PREPARATION OF 7-OXABICYCLO[4.3.0]NONANES AND 2-OXABICYCLO[4.4.0]DECANES SPECIFICALLY LABELLED WITH DEUTERIUM

František Tureček

*Jaroslav Heyrovský Institute of Physical Chemistry and Electrochemistry, Czechoslovak Academy of Sciences, 121 38 Prague**

Received July 21st, 1981

trans-Annulated 7-oxabicyclo[4,3,0]nonanes, labelled with deuterium at $C_{(1)}$, $C_{(6)}$, $C_{(8)}$ and $C_{(9)}$, and *cis*-annulated isomers labelled at $C_{(1)}$ and $C_{(6)}$ were prepared by cyclization of the corresponding labelled 2-(2-hydroxyethyl)-cyclohexanols. *cis*-Annulated 7-oxabicyclo[4,3,0]-nonanes labelled at $C_{(5)}$, $C_{(8)}$ and $C_{(9)}$ were prepared by oxymercuration-reduction of labelled 2-(3-cyclohexenyl)ethanols. 2-Oxabicyclo[4.4.0]decanes labelled at $C_{(1)}$, $C_{(3)}$ and $C_{(6)}$ were prepared by cyclization of the corresponding 2-(3-hydroxypropyl)cyclohexanols. *cis*-Annulated 2-oxabicyclo[4,4,0]decanes labelled at $C_{(4)}$, $C_{(5)}$ and $C_{(10)}$ were obtained by oxymercuration--reduction of 3-(3-cyclohexenyl)-propanols. Conformation of the *cis*-annulated isomers is discussed.

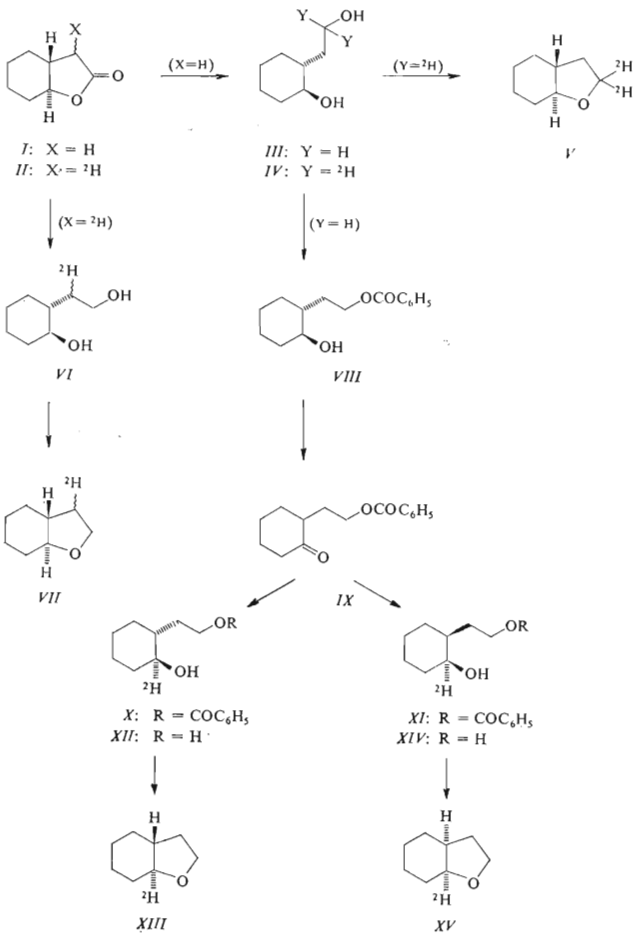
For a study of the stereoelectronic effect on decompositions of organic ions in the gas phase we needed a series of *cis* and *trans*-annulated 7-oxabicyclo[4.3.0]nonanes and 2-oxabicyclo[4.4.0]decanes with a well-defined position of the deuterium label on the skeleton. Preparation of the former compounds has been described earlier[1-3]; however, the methods used are neither suitable for specific introduction of deuterium, nor provide good yields. 2-Oxabicyclo[4.4.0]decanes have been prepared by hydrogenation of chroman[4] or mentioned as by-products of cyclization of 2-allylcyclohexanols[5]. However, neither of the literature procedures makes it possible to introduce deuterium in a specific manner. In the present paper we report preparations which make use of stereospecific reactions to create the desired annulation of the skeleton and which are also suitable for specific labelling of 1-, 5-, 6-, 8- and 9-positions in 7-oxabicyclo[4.3.0]nonanes and 1-, 3-, 4-, 5-, 6- and 10-positions in 2-oxabicyclo--[4.4.0]decanes.

The synthesis of the *trans*-annulated [8,8-$^2H_2$]derivative *V* started from the elacton *I* (ref.[6]). Reduction of *I* with lithium aluminum deuteride afforded the diol *IV* which was further cyclized, *via* an unstable monotosylate, with 1,4-diazabicyclo-

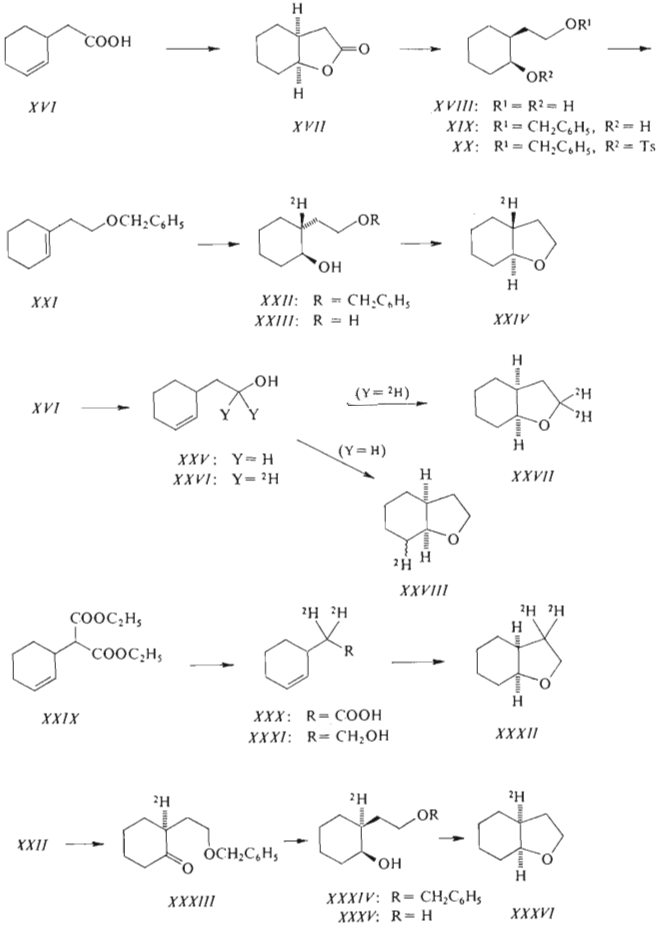
* Present address: Cornell University, Baker Laboratory, Ithaca, NY 14853 USA.

[2.2.2]octane to yield the ether *V* (Scheme 1). On deuteriation (lithium diisopropyl amide, N,N,N′,N′-tetramethylethylenediamine, deuterium oxide) *I* gave the labelled lactone *II* which was reduced to the diol *VI* and the latter compound was cyclized to the [9-^{2}H]derivative *VII*. The preparation of the [6-^{2}H]derivative *XIII* also started from *I*. Reduction of *I* furnished the diol *III* (ref.[2]), in which the primary hydroxy group was protected as the monobenzoate *VIII* and then the secondary hydroxyl was oxidized with pyridinium chlorochromate[7–10] to yield the ketone *IX* (Scheme 1). Reduction of *IX* with sodium borodeuteride afforded a mixture of *trans* and *cis*-alcohols *X* and *XI*, respectively, which were separated by column chromatography. After removal of the protecting group, the diol *XII* was cyclized *via* a monotosylate to the *trans*-annulated [6-^{2}H]derivative *XIII*. The *trans*-annulated [1-^{2}H]-derivative *XXIV* was prepared from (3-cyclohexenyl)acetic acid[11] (*XVI*, Scheme 2). Iodolactonization[12] of *XVI* followed by reduction with tri-n-butyltin hydride[13] furnished the *cis*-annulated lactone *XVII* (ref.[14]), which was reduced with lithium aluminum hydride to the diol *XVIII*. After having protected the primary hydroxy group as the benzyl ether *XIX*, the secondary hydroxyl was tosylated (*XX*) and the tosyloxy group was eliminated with 1,8-diazabicyclo[5.4.0]-7-undecene. Elimination of the axial tosyloxy group furnished the single olefin *XXI* in which the position of the double bond made it possible to place deuterium specifically at $C_{(1)}$. On deuterioboration-oxidation of the double bond in *XXI* we obtained the *trans*-alcohol *XXII* which was converted to the diol *XXIII*. The removal of the benzyl group in *XXII* left the deuterium label intact, as corroborated by comparing the label contents in *XXII* and *XXIII*. The [1-^{2}H]derivative *XXIV* was prepared from *XXIII* *via* a monotosylate, as described above. The purity of the *trans*-annulated ethers *V*, *VII*, *XIII*, and *XXIV*, as well as their deuterium contents, were checked by gas chromatography–mass spectrometry. Each *trans*-annulated compound contained about 1–3% of the corresponding *cis*-isomer. The formation of the *cis*-isomers is probably due to imperfect regiospecificity of tosylation of diols *IV*, *VI*, *XXII* and *XXIII* in which the equatorial hydroxyl group is tosylated to a small extent, too. Intramolecular nucleophilic substitution of the secondary tosyloxy group by the primary hydroxyl results in configurational inversion at $C_{(6)}$ and leads to the *cis*-annulated isomer.

The annulation and deuterium position in *V*, *VII*, *XIII* and *XXIV* were confirmed by ^{1}H NMR spectra. The signals of protons at $C_{(6)}$ ($H_{(6)}$) and $C_{(8)}$($H_{(8)}$, $H_{(8')}$) are well-resolved at 200 MHz. In the spectrum of *trans*-7-oxabicyclo[4.3.0]nonane[1] the signal of the $H_{(6)}$ proton appears as a doublet of doublets of doublets at $\delta = 2{\cdot}96$, while the signals of $H_{(8)}$ and $H_{(8')}$ appear as multiplets at $\delta = 3{\cdot}94$ and $\sigma = 4{\cdot}31$, respectively. In the spectrum of *V* the latter signals vanish, while with *VII* their shape is changed only. With *XIII* the signal of $H_{(6)}$ is absent, while with *XXIV* the latter signal appears as a doublet of doublets, the line-width being broadened considerably by ^{1}H—^{2}H interaction.

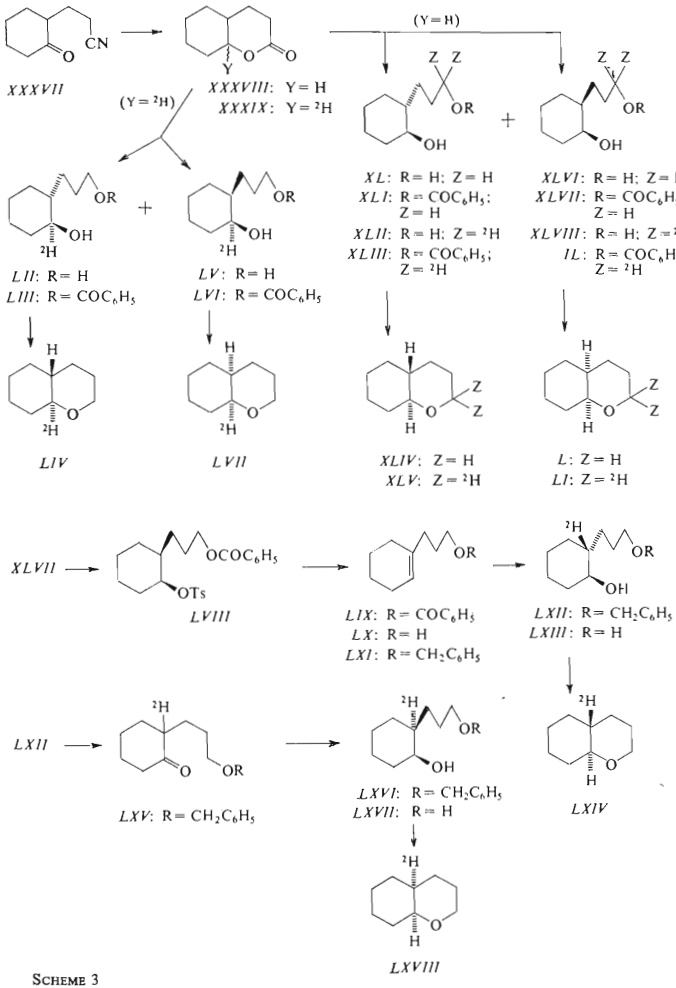

(X=H)
(Y=²H)
I: X = H
II: X = ²H
III: Y = H
IV: Y = ²H
V
(X=²H)
(Y=H)
VI
VIII
VII
IX
X: R = COC₆H₅
XII: R = H
XI: R = COC₆H₅
XIV: R = H
XIII
XV

SCHEME 1


COOH
XVI
H
O
O
H
XVII
OR¹
OR²
XVIII: R¹ = R² = H
XIX: R¹ = CH₂C₆H₅, R² = H
XX: R¹ = CH₂C₆H₅, R² = Ts
OCH₂C₆H₅
XXI
²H
OR
OH
XXII: R = CH₂C₆H₅
XXIII: R = H
²H
O
H
XXIV
XVI
OH
Y Y
XXV: Y = H
XXVI: Y = ²H
(Y = ²H)
(Y = H)
H
²H
O
²H H
XXVII
XXVIII
COOC₂H₅
COOC₂H₅
XXIX
²H ²H
R
XXX: R = COOH
XXXI: R = CH₂OH
²H ²H
H
O
H
XXXII
XXII
²H
O
OCH₂C₆H₅
XXXIII
²H
OR
OH
XXXIV: R = CH₂C₆H₅
XXXV: R = H
²H
O
H
XXXVI

SCHEME 2

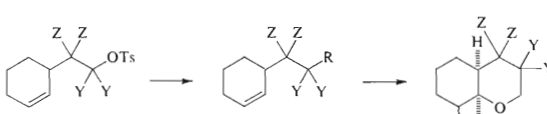
Preparation of *cis*-annulated ethers *XXVII*, *XXVIII* and *XXXII* was based on intramolecular participation of the hydroxy group[5] in oxymercuration of 2-(3-cyclohexenyl)ethanol (Scheme 2). Reduction of the acid *XVI* with lithium aluminum deuteride furnished the alcohol *XXVI* which on oxymercuration with mercuric acetate and subsequent reduction with sodium borohydride gave the [8,8-$^2H_2$]derivative *XXVII* in high yield. The [5-^{2}H]derivative *XXVIII* was prepared from the alcohol *XXV* (ref.[11]), by reducing the organomercuric intermediate with sodium borodeuteride. The 9-position was labelled as follows: The malonic ester *XXIX* (ref.[11]) was hydrolyzed with deuterium oxide and the resulting (3-cyclohexenyl)-malonic acid was decarboxylated to afford the labelled acid *XXX*. Reduction of *XXX* furnished the alcohol *XXXI* which was cyclized to the [9,9-$^2H_2$]derivative *XXXII*. Syntheses of the *cis*-annulated ethers *XV* and *XXXVI* made use of the intermediates obtained in the synthesis of the *trans*-annulated isomers. Thus, the benzoate *XI*, obtained by reduction of the ketone *IX* with sodium borodeuteride, was converted to the diol *XIV* and the latter was cyclized *via* a monotosylate to the *cis*-[6-^{2}H]-derivative *XV*. Oxidation of the labelled alcohol *XXII* afforded the ketone *XXXIII* which was reduced with lithium tri-s-butyl borohydride[10] to the *cis*-alcohol *XXXIV*. After this *trans*-to-*cis* conversion, the protective group was removed by hydrogenation and the resulting diol *XXXV* was cyclized *via* a monotosylate to the *cis*-annulated [1-^{2}H]derivative *XXXVI*. The purity and deuterium content in the *cis*-annulated ethers were checked by gas chromatography-mass spectrometry. Both the oxymercuration-reduction of 2-(3-cyclohexenyl) ethanols and the cyclization of *cis*-diols afforded products of high purity, usually better than 99%. The position of the label and the ring junction were confirmed by ^{1}H NMR spectroscopy. The *cis*-annulated 7-oxabicyclo[4.3.0]nonane skeleton can, *a priori*, adopt two stable conformations, the $C_{(6)}$—O bond being either axial or equatorial with respect to the six-membered ring. In the ^{1}H NMR spectrum of unlabelled *cis*-7-oxabicyclo[4.3.0]nonane[3], the signal of one proton at $C_{(8)}$ ($H_{(8)}$, $\delta = 3{\cdot}96$) is distinct, while the singal of the $H_{(8')}$ proton ($\delta = 3{\cdot}80$) overlaps with that of the angular proton $H_{(6)}$ ($\delta = 3{\cdot}81$). In the spectrum of the [8,8-$^2H_2$]derivative, the signal of the $H_{(6)}$ proton appears as a doublet of doublets of doublets ($J = 3{\cdot}9$ Hz) at $\delta = 3{\cdot}81$. The chemical shift and vicinal coupling constants of $H_{(6)}$ indicate that the *cis*-annulated skeleton adopts preferentially the conformation with an axial position of the $C_{(6)}$—O bond. This means, however, that the configuration of deuterium at $C_{(5)}$ (compound *XXVIII*) cannot be determined from ^{1}H NMR spectra, due to very similar vicinal coupling constants $J_{5,6}$ and $J_{5',6}$. Nevertheless, the signal of the $H_{(6)}$ proton in the spectrum of *XXVIII* shows only three bands, thus confirming the location of deuterium at $C_{(5)}$. In the ^{1}H NMR spectrum of the [9,9-$^2H_2$]derivative *XXXII* the multiplets of the $H_{(8)}$ and $H_{(8')}$ protons are reduced to doublets, but the bands are considerably broadened by ^{1}H—^{2}H coupling. The ^{1}H NMR spectra of *XV* and *XXXVI* agree well with the supposed position of deuterium on the skeleton.


XXXVII
XXXVIII: Y = H
XXXIX: Y = ²H
(Y = H)
(Y = ²H)
XL: R = H; Z = H
XLI: R = COC₆H₅; Z = H
XLII: R = H; Z = ²H
XLIII: R = COC₆H₅; Z = ²H
XLVI: R = H; Z = H
XLVII: R = COC₆H₅; Z = H
XLVIII: R = H; Z = ²H
IL: R = COC₆H₅; Z = ²H
LII: R = H
LIII: R = COC₆H₅
LV: R = H
LVI: R = COC₆H₅
LIV
LVII
XLIV: Z = H
XLV: Z = ²H
L: Z = H
LI: Z = ²H
XLVII
LVIII
LIX: R = COC₆H₅
LX: R = H
LXI: R = CH₂C₆H₅
LXII: R = CH₂C₆H₅
LXIII: R = H
LXII
LXV: R = CH₂C₆H₅
LXVI: R = CH₂C₆H₅
LXVII: R = H
LXIV
LXVIII

SCHEME 3

The preparation of 2-oxabicyclo[4.4.0]decanes and their labelled derivatives started from 3-(2-oxocyclohexyl)propannitrile (*XXXVII*, ref.[8]) which was converted to a mixture of *cis*- and *trans*-annulated lactones *XXXVIII* (ref.[9], Scheme 3). This procedure is also suitable for introduction of deuterium to the 1-position of the six membered ring (lactones *XXXIX*). On reduction of lactones *XXXVIII* with lithium aluminum hydride we obtained a mixture of diols *XL* and *XLVI* (ref.[9]) which were separated by column chromatography as monobenzoates *XLI* and *XLVII*, respectively. vely. The protecting group was removed by hydrolysis and the pure diols *XL* and *XLVI* were cyclized *via* the corresponding monotosylates to *trans* and *cis*-annulated ethers *XLIV* and *L*, respectively. The same procedure was employed to prepare the [1-^{2}H]derivatives *LIV* and *LVII* (Scheme 3), and [3,3-$^2H_2$]derivatives *XLV* and *LI*. The *cis*-benzoate *XLVII* was further used as a starting compound for the synthesis of [6-^{2}H]derivatives *LXIV* and *LXVIII*. On tosylation (compound *LVIII*) and subsequent elimination of the tosyloxy group we obtained the unsaturated benzoate *LIX*. Again, the elimination of the axial tosyloxy group proceeded cleanly, furnishing the single olefin *LIX*. After exchange of protecting groups: benzoate *LIX* → alcohol *LX* (ref.[15-17]) → benzyl ether *LXI*, the double bond in *LXI* was deuterioborated to produce the *trans*-alcohol *LXII*. The benzyl group in *LXII* was removed by hydrogenation and the diol *LXIII* was cyclized *via* a monotosylate to furnish the *trans*--annulate [6-^{2}H]derivative *LXIV*. The *cis*-annulated isomer *LXVIII* was prepared from the benzyl ether *LXII*. Oxidation of *LXII* with pyridinium chlorochromate[7] afforded the ketone *LXV* which was reduced with lithium tri-s-butyl borohydride[10] o the *cis*-alcohol *LXVI*. The benzyl group in *LXVI* was removed by hydrogenation and the diol *LXVII* was cyclized to the *cis*-annulated [6-^{2}H]derivative *LXVIII*.

The *cis*-annulated ethers *LXXV*, *LXXIX* and *LXXXIII* were prepared by procedure which started from alcohols *XXV*, *XXVI* and *XXXI* (Scheme 1 and 4). Extending the side chain in *XXV* by the reaction sequence: alcohol *XXV* → tosylate *LXIX* → → nitrile *LXXII* → acid *LXXIII* (ref.[12]) → alcohol *LXXIV*, and quite analogously for the labelled derivatives (Scheme 4), we obtained the intermediates *LXXIV*, *LXXVIII* and *LXXXII* which were suitable for a stereospecific formation of the *cis*--annulated skeleton. Oxymercuration of *LXXIV*, followed by reduction with sodium borodeuteride, afforded the *cis*-annulated [10-^{2}H]derivative *LXXV*. In a similar manner, the alcohols *LXXVIII* and *LXXXII* were converted to the *cis*-annulated [4,4-$^2H_2$] and [5,5-$^2H_2$]derivatives *LXXIX* and *LXXXIII*, respectively, using sodium borohydride as a reducing agent. The ring junction and deuterium integrity of all 2-oxabicyclo[4.4.0]decanes were checked by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of the *trans*-isomer *XLIV* displays the signals of protons at $C_{(1)}$ ($H_{(1)}$, δ = = 2·89) and $C_{(3)}$ ($H_{(3)}$, δ = 3·97 and $H_{(3')}$, δ = 3·44). Hence, the presence of deuterium at $C_{(1)}$, $C_{(3)}$ and $C_{(6)}$ can be followed easily and the ^{1}H NMR spectra of *XLV*, *LIV* and *LXIV* agreed well with the assumed sites of labelling. In the ^{1}H NMR spectrum of the *cis*-annulated isomer *L*, the signals of $H_{(3)}$ (δ = 3·98) and $H_{(3')}$ (δ = 3·45)



LXIX: Y = Z = H
LXX: Y = ^{2}H; Z = H
LXXI: Y = H; Z = ^{2}H

LXXII: Y = Z = H; R = CN
LXXIII: Y = Z = H; R = COOH
LXXIV: Y = Z = H; R = CH_2OH
LXXVI: Y = ^{2}H; R = H; R = CN
LXXVII: Y = ^{2}H; Z = H; R = COOH
LXXVIII: Y = ^{2}H; Z = H; R = CH_2OH
LXXX: Y = H; Z = ^{2}H; R = CN
LXXXI: Y = H; Z = ^{2}H; R = COOH
LXXXII: Y = H; Z = ^{2}H; R = CH_2OH

LXXV: Y = Z = H; R = ^{2}H
LXXIX: R = Z = H; Y = ^{2}H
LXXXIII: R = Y = H; Z = ^{2}H

SCHEME 4

protons are discerned from the signal of the $H_{(1)}$ proton (δ = 3·54, ddd, J = 3·0 Hz). The chemical shift and vicinal coupling constants of the angular proton $H_{(1)}$ indicate that the *cis*-annulated 2-oxabicyclo[4.4.0]decane skeleton prefers the conformation with an axial position of the $C_{(1)}$—O bond on the carbocyclic six-membered ring. This conclusion is also consistent with earlier results obtained from conformational analysis of *cis*-annulated perhydroquinolines[16].

EXPERIMENTAL

Melting points were determined on a Boetius melting-point apparatus. The refractive indices were measured on an Abbe refractometer. The infrared (IR) spectra were recorded on a UR-20 Zeiss (Jena) spectrometer in neat film. The ^{1}H NMR spectra were measured on a Varian XL-200 spectrometer (200·05 MHz, FT-mode) at 25°C or on a Tesla BS-467 instrument (60 MHz) in deuteriochloroform with tetramethylsilane as an internal reference. The chemical shifts are are expressed in δ (ppm) scale, the apparent coupling constants were obtained by first-order analysis. The mass spectra were recorded ona JEOL JMS D-100 spectrometer at 75 eV. The samples were introduced *via* a direct inlet system or by using the gas chromatograph-mass spectrometer coupling (column: SE-30, 3% on Chromosorb W, jet separator Becker-Ryhage). The reaction course and purity of products were checked by thin-layer chromatography on Merck Kieselguhr plates or by gas chromatography–mass spectrometry. The deuterium content in label-

led compounds was determined by mass spectrometry. The expression "worked up" means that the extract was washed successively with 5% hydrochloric acid, 5% sodium carbonate solution, water, dried over sodium sulphate and the solvent was distilled off through a 20 cm Vigreux column.

trans-2-(2-[2,2-$^2H_2$]Hydroxyethyl)cyclohexanol (*IV*)

A solution of the lactone *I* (1 g, 7·1 mmol) in ether (10 ml) was added to a slurry of lithium aluminum deuteride (170 mg, 4 mmol) in ether (10 ml). After 20 min, stirring, the excess of deuteride was destroyed with a saturated solution of sodium sulphate and the ethereal solution was worked up. Distillation afforded 980 mg (95%) of the diol *IV*, b.p. 95–96°C/27 Pa (ref.[2] gives b.p. 104–105°C/133 Pa for the non-labelled compound). ^{1}H NMR spectrum: 4·16 (s, 2 H), 3·21 (ddd, J = 9·8, 9·8, and 4·4 Hz, 1 H), 1·96 (m, 1 H), 1·72 (m, 5 H), 1·21 (m, 5 H).

trans-[8,8-$^2H_2$]-7-Oxabicyclo[4,3,0]nonane (*V*)

p-Toluenesulphonyl chloride (690 mg, 3·6 mmol) was added at −40°C to a solution of the diol *IV* (500 mg, 3·5 mmol) in pyridine (5 ml). After 12 h standing at −5°C the mixture was additioned with dichloromethane (20 ml), the solution was poured into water and worked up. The residue was dissolved in dimethyl formamide (5 ml), 1,4-diazabicyclo[2.2.2]octane was added (500 mg) and the mixture was heated under argon at 90°C for 2 h. After cooling pentane was added, the mixture was poured into water and the pentane solution worked up. Distillation gave 200 mg (46%) of *V*, b.p. 85–88°C/8 kPa, n_D^{20} = 1·4647 (ref.[2] gives n_D^{25} = 1·4632 for the non-labelled compound). ^{1}H NMR spectrum: 2·96 (ddd, J = 9·7, 0·7 and 3·8 Hz, 1 H), 2·01 (m, 6 H), 1·83 (m, 1 H), 1·73 (m, 1 H), 1·30 (m, 3 H); mass spectrum (*m/z*, rel. intensity): 128 (23), 127(15), 126 (1), 99 (4), 85 (100), 84 (8), 67 (18), 57 (13), 55 (9). Deuterium content: 89·5% $^2H_2$, 10·5% $^2H_1$, 1% $^2H_0$.

trans-[9-^{2}H]-7-Oxybicyclo[4,3,0]nonan-8-one (*II*)

A solution of the lactone *I* (1·5 g, 10·7 mmol) in tetrahydrofuran (15 ml) was added at −40°C and under argon to a solution of lithium diisopropyl amide (20 mmol) in N,N,N′,N′-tetramethylethylenediamine (5 ml) and tetrahydrofuran (10 ml). The mixture was stirred 4 h at −40°C, then warmed to 0°C (2 h) and quenched with deuterium oxide (1 ml). The solution was made neutral with [O—^{2}H]trifluoroacetic acid, the product was taken up with ether and worked up. Distillation afforded 800 mg (53%) of *II*, b.p. 130–140°C/1·6 kPa. ^{1}H NMR spectrum: 3·86 (ddd, J = 10·8, 10·8 and 3·9 Hz), 1 H), 2·27 (m, 1 H), 1·97 (m, 3 H), 1·84 (m, 2 H), 1·37 (m, 4 H); IR spectrum (cm^{-1}): 2 130, 1 799, 1 745, 1 214, 1 195, 1 133, 1 082, 1 038, 960, 937, 878, 700; mass spectrum (*m/z*, rel. intensity): 141 (4), 140 (2·5), 139 (2), 123 (4), 122 (3), 97 (17), 81 (22), 69 (31), 68 (43), 67 (100), 55 (37), 41 (48), 39 (31).

trans-2-(2-[1-^{2}H]Hydroxyethyl)cyclohexanol (*VI*)

Was prepared from *II* as described for *IV*. ^{1}H NMR spectrum: 4·14 (s, 2 H), 3·59–3·75 (m, 1·2 H), 3·20 (ddd, J = 9·8., 9·8 and 4·4 Hz, 1 H).

trans-[9-^{2}H]-7-Oxabicyclo[4.3.0]nonane (*VII*)

Was prepared from *VI* as described for *V*. ^{1}H NMR spectrum: 4·31 (m, 1 H), 3·94 (m, 1 H), 2·96 (ddd, J = 9·7, 9·7 and 3·8 Hz, 1 H), 2·01 (m, 5 H), 1·83 (m, 1 H), 1·73 (m, 1 H), 1·30 (m, 3 H)

mass spectrum (*m/z*, rel. intensity): 128 (6), 127 (6), 127 (27), 126 (24), 125 (6), 98 (6), 85 (21), 84 (100), 83 (50), 67 (25), 56 (18), 55 (22). Deuterium content: 9% $^2H_2$, 61% $^2H_1$, 30% $^2H_0$.

trans-2-(2-Hydroxyethyl)cyclohexanol Monobenzoate (*VIII*)

Benzoyl chloride (3·5 g) in ether (10 ml) was added at −40°C over 1 h to asolution of the diol *III* (3·4 g, 23·6 mmol) in pyridine (10 ml) and ether (5 ml). After standing for 1 h at −40°C and 6 h at −5°C the mixture was poured into water, the product extracted with ether and worked up. The crude product was purified by column chromatography (silica gel, light petroleum–ether, 1 : 1). Yield 4·8 g (82%) of oily *VIII*; IR spectrum (cm^{-1}): 3 620, 3 400, 1 735, 1 605, 1 497, 1 080, 1 040; ^1H NMR spectrum: 8·05 (m, 2 H), 7·40—7·59 (m, 3 H), 4·36 (m, 2 H), 3·21 (ddd, J = 9·7, 9·7 and 4·5 Hz, 1 H).

trans-2-(2-Benzoyloxyethyl)cyclohexanone (*IX*)

Alcohol *VIII* (4·7 g, 18·9 mmol) in dichloromethane (20 ml) was oxidized with pyridinium chlorochromate (10 g). After 4 h stirring the conversion was complete, the mixture was worked up[7] to yield 4·3 g (92%) of oily *IX*. For $C_{15}H_{18}O_3$ (246·3) calculated; 73·15% C, 7·37% H; found: 73·38% C, 7·22% H. IR spectrum (cm^{-1}): 1 735, 1 700.

trans,cis-[1-^{2}H]-2-(2-Benzoyloxyethyl)cyclohexanols (*X* and *XI*)

Ketone *IX* (4·25 g, 17·2 mmol) in ethanol (20 ml) was reduced with sodium borodeuteride (240 mg, 6 mmol) at 0°C for 30 min. The mixture was diluted with ether (100 ml), poured into water and worked up. The mixture of *X* and *XI* was separated on a silica gel column (elution with light petroleum–ether, 2 : 1) to yield *X* (1·3 g) and *XI* (1·35 g, higher R_F-value). *X* was identified by comparison of its R_F-value with that of *VIII*.

trans-[1-^{2}H]-2-(2-Hydroxyethyl)cyclohexanol (*XII*)

The benzoate *X* (1·3 g) was dissolved in a solution of potassium hydroxide in methanol (5 ml) and water (1 ml) and the mixture was refluxed for 6 h. Methanol was evaporated *in vacuo*, the product was extracted with ether and worked up. Distillation yielded 710 mg (93%) of *XII*, b.p. 95—100°C/26 Pa. ^1H NMR spectrum: 4·14 (s, 2 H), 3·75 (m, 1 H), 3·59 (m, 1 H); mass spectrum (*m/z*, rel. intensity): 145 (19), 127 (13), 126 (17), 110 (13), 109 (22), 99 (59), 98 (93), 97 (37), 67 (100), 58 (71), 55 (100), 42 (54), 41 (98), 31 (37).

cis-[1-^{2}H]-2-(2-Hydroxyethyl)cyclohexanol (*XIV*)

Was prepared from *XI* as described for *XII*. ^1H NMR spectrum: 3·67 (m, 2 H), 2·89 (s, 2 H), 1·38 (m, 11 H); mass spectrum (*m/z*, rel. intensity): 145 (17), 127 (11), 126 (19), 110 (13), 109 (22), 99 (57), 98 (95), 97 (40), 67 (100), 58 (73), 55 (98), 41 (97), 31 (40).

trans-[6-^{2}H]-7-Oxabicyclo[4,3,0]nonane (*XIII*)

Was prepared from *XII* as described for *V*. Yield 51%, n_D^{20} = 1·4638. ^1H NMR spectrum: 4·31 (m, 1 H), 3·94 (m, 1 H), 2·02 (m, 6 H), 1·883 (m, 1 H), 1·74 (m, 1 H), 1·32 (m, 3 H); mass spectrum (*m/z*, rel. intensity): 127 (22), 126 (3), 125 (7), 98 (4), 84 (100), 83 (9), 67 (16), 56 (9), 55 (15). Deuterium content: 93% $^2H_1$, 7% $^2H_0$.

cis-[6-^{2}H]-7-Oxabicyclo[4,3,0]nonane (*XV*)

Was prepared from *XIV* as described for *V*. Yield 47%, $n_D^{20} = 1{\cdot}4663$. ^{1}H NMR spectrum: 3·96 (m, 1 H), 3·80 (m, 1 H), 2·03 (m, 2 H), 1·90 (m, 1 H), 1·60 (m, 4 H), 1·46 (m, 2 H), 1·27 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 127 (23·5), 126 (2), 125 (3), 98 (3·5), 84 (100), 83 (9), 67 (6), 56 (9), 55 (11). Deuterium content: 93% $^2H_1$, 7% $^2H_0$.

cis-2-(2-Hydroxyethyl)cyclohexanol (*XVIII*)

cis-Lactone *XVII* (4·2 g, 30 mmol) in ether (20 ml) was added to a slurry of lithium aluminum hydride (800 mg, 21 mmol) in ether (20 ml). The mixture was refluxed for 2 h, excessive hydride was decomposed by saturated sodium sulphate solution and the ethereal solution worked up. Distillation gave 4·1 g (95%) of *cis*-diol *XVIII*, b.p. 110—112°C/130 Pa. For $C_8H_{16}O_2$ (144·2) calculated: 66·63% C, 11·18% H; found: 66·36% C, 11·24% H. ^{1}H NMR spectrum: 3·81 (m, $W = 9{\cdot}5$ Hz, 1 H), 3·61 (m, 2 H), 2·89 (s, 2 H), 1·38 (m, 10 H); mass spectrum (*m/z*, rel. intensity): 144 (11), 126 (12), 111 (6), 108 (14), 101 (31), 98 (75), 93 (34), 83 (65), 82 (53), 70 (47), 67 (96), 57 (72), 55 (91), 41 (100), 31 (36); IR spectrum (cm^{-1}): 3 360, 1 458, 1 145, 1 060, 1 015, 990, 970, 885.

1-(2-Benzyloxyethyl)cyclohexene (*XXI*)

Benzyl bromide (4·9 g, 28·7 mmol) in tetrahydrofuran (10 ml) was added dropwise to a refluxing solution of the diol *XVIII* (4·05 g, 28·1 mmol) and sodium hydride (1 g, 41·6 mmol) in tetrahydrofuran (40 ml). After 4 h refluxing ether (100 ml) was added, sodium hydride was decomposed with water (100 ml) and the ethereal solution was worked up. The crude benzyl ether *XIX* (6·7 g) was treated with *p*-toluenesulphonyl chloride (5·7 g) in pyridine (25 ml) at 20°C for 24 h. The mixture was diluted with ether, poured into water and worked up. The crude tosylate *XX* (8·9 g, 88%) was dissolved in dioxan (20 ml), 1,8-diazabicyclo[5.4.0]-7-undecene (4·4 g) was added and the solution was refluxed under argon for 2 h. Light petroleum was added, the mixture was poured into water and the organic phase worked up. Distillation afforded 3 g (63%) of *XXI*, b.p. 110—115°C/30 Pa, $n_D^{20} = 1{\cdot}5218$. For $C_{15}H_{20}O$ (216·2) calculated: 83·29% C, 9·32% H: found: 83·15% C, 9·32% H. ^{1}H NMR spectrum: 7·30 (s, 5 H), 5·47 (m, 1 H), 4·15 (s, 2 H), 3·51 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 216 (4), 198(1), 160 (3), 125 (18), 110 (22), 107 (41), 95 (18), 91 (100), 81 (25), 79 (34); IR spectrum (cm^{-1}): 3 080, 3 060, 1 507, 1 465, 1 370, 1 110, 740, 705.

trans-[2-^{2}H]-2-(2-Benzyloxyethyl)cyclohexanol (*XXII*)

Boron trifluoride etherate (1·33 g, 9·4 mmol) in tetrahydrofuran (10 ml) was added dropwise under argon to a cooled (0°C) mixture of the benzyl ether *XXI* (3 g, 13·9 mmol) and lithium aluminum deuteride (280 mg, 7 mmol) in tetrahydrofuran (15 ml). After 2 h stirring at 20°C the excessive deuteride was decomposed with water and the mixture was treated with 3M-NaOH (5 ml) and 30% hydrogen peroxide (5 ml) at 60°C for 2 h. Ether was added (60 ml) and the ethereal solution was worked up. Yield 3·0 g (92%). ^{1}H NMR spectrum: 7·34 (s, 5 H), 4·53 (s, 2 H), 3·55 (m, 2 H), 3·20 (m, $W = 16$ Hz, 1 H), 1·65 (m, 10 H); mass spectrum (*m/z*, rel. intensity): 235 (0·5), 217 (2), 199 (0·7), 144 (4·5), 129 (6), 126 (16), 111 (10), 108 (15), 107 (27), 92 (24), 91 (100), 82 (30), 65 (14); IR spectrum (cm^{-1}): 3 610, 3 420, 3 080, 3 045, 2 130, 1 505, 1 460, 1 370, 1 213, 1 105, 1 085, 1 060, 1 035.

trans-[2-^{2}H]-2-(2-Hydroxyethyl)cyclohexanol (*XXIII*)

Benzyl ether *XXII* (950 mg) in ethanol (50 ml) was hydrogenated on palladium catalyst (100 mg) at 20°C for 2 h. The catalyst was filtered off, ethanol was evaporated *in vacuo* and the residue purified by distillation. Yield: 580 mg (95%), b.p. 96–98°C/30 Pa. ^{1}H NMR spectrum: 3·75 (m, 4 H, 3·21 (m, W = 16 Hz, 1 H), 1·25–2·00 (m, 10 H); mass spectrum (m/z, rel. intensity): 145 (13), 127 (14), 109 (15), 108 (8), 101 (31), 99 (74), 83 (100), 68 (74), 67 (72), 57 (60), 56 (65), 55 (87), 42 (640), 41 (76), 31 (38).

trans-[1-^{2}H]-7-Oxabicyclo[4.3.0]nonane (*XXIV*)

Was prepared from *XXIII* as described for *V*. Yield 48%, n_D^{20} = 1·4636; ^{1}H NMR spectrum: 4·31 (m, 1 H), 3·4 (m, 1 H), 2·95 (dd, J = 9·7 and 3·8 Hz), 2·00 (m, 5 H), 1·83 (m, 1 H), 1·73 (m, 1 H), 1·30 (m, 3 H); mass spectrum (m/z, rel. intensity): 127 (25), 126 (14), 125 (1), 98 (3), 97 (4), 84 (8), 83 (100), 68 (9), 67 (15), 56 (12), 55 (16). Deuterium content: 95% $^2H_1$, 5% $^2H_0$.

[1,1-$^2H_2$]-2-(3-Cyclohexenyl)ethanol (*XXVI*)

A solution of the acid *XIV* (2 g, 14·3 mmol) in ether (20 ml) was added dropwise to a slurry of lithium aluminum deuteride (600 mg, 14·2 mmol) in ether (20 ml). After 2 h refluxing the excess of deuteride was decomposed with a saturated sodium sulphate solution, and the ethereal solution was worked up. Distillation gave 1·75 g (95%) of *XXVI*, b.p. 95–100°C/1·6 kPa, n_D^{20} = = 1·4879 (ref.[11] gives b.p. 100–101°C/80 Pa, n_D^{25} = 1·4863 for the non-labelled compound).

cis-[8,8-$^2H_2$]-7-Oxabicyclo[4.3.0]nonane (*XXVII*)

Alcohol *XXVI* (300 mg, 2·3 mmol) in tetrahydrofuran (3 ml) was added to a suspension of mercuric acetate (1 g) in tetrahydrofuran (2 ml) and water (1 ml). The mixture was stirred for 12 h and then treated with a solution of sodium hydroxide (0·8 g) and sodium borohydride (150 mg) in water (6 ml). After 10 min, stirring the product was extracted with pentane (15 ml), the extract was washed with water, saturated calcium chloride solution and worked up. Distillation gave 200 mg (66%) of *XXVII*, b.p. 85–88°C/8 kPa, n_D^{20} = 1·4664 (ref.[1] gives n_D^{24} = 1·4648 for the non-labelled compound). ^{1}H NMR spectrum: 3·81 (ddd, J = 3·9, 3·9 and 3·9 Hz, 1 H), 1·93 (m, 3 H), 1·57 (m, 6 H), 1·23 (m, 2 H); mass spectrum (m/z, rel. intensity): 128 (17·5), 127 (4·5), 126 (0·3), 99 (3), 86 (4·5), 85 (100), 84 (6), 67 (5), 57 (10), 55 (6). Deuterium content: 94·5% ^{2}H, 4·5% $^2H_1$, 1% $^2H_0$.

cis-[5-^{2}H[-7-Oxabicyclo[4,3,0]nonane (*XXVIII*)

Was prepared from 2-(3-cyclohexenyl)ethanol (*XXV*) analogously as described for *XXVII*. Sodium borodeuteride was used to reduce the organomercuric intermediate. Yield 74%, n_D^{20} = = 1·4660. ^{1}H NMR spectrum: 3·96 (ddd, J = 8·2, 7·4 and 7·4 Hz, 1 H), 3·81, 3·80 (m, 2 H), 2·01 (m, 2 H), 1·87 (m, 1 H), 1·58 (m, 3 H), 1·44 (m, 2 H), 1·25 (m, 2 H); mass spectrum (m/z, rel. intensity): 127 (17), 126 (5), 125 (0·2), 97 (3), 84 (5), 83 (100), 69 (4), 68 (5), 67 (3), 55 (13). Deuterium content: 93% $^2H_1$, 7% $^2H_0$.

[2,2-$^2H_2$]-2-(3-Cyclohexenyl)acetic Acid (*XXX*)

A solution of ethyl-2-(3-cyclohexenyl) malonate[11] (7·5 g, 31 mmol), sodium deuteroxide (4·16 g) and triethylbenzylammonium chloride (200 mg) in deuterium oxide (15 ml) was refluxed under

argon for 24 h. The mixture was acidified with [$^2H_3$] phosphoric acid, the malonic acid was filtered off by surion, dried over phosphoct pentoxide and then decomposed at 200–220°C/2 kPa. The product was redistilled to yield 3·6 g (83%) of *XXX*, b.p. 151°C/2 kPa, $n_D^{20} = 1{\cdot}4847$ (ref.[11] gives b.p. 116°C/13 Pa, $n_D^{26} = 1{\cdot}4828$ for the non-labelled compound). Mass spectrum (*m/z*, rel. intensity): 143 (3), 142 (4·7), 141 (1), 125 (6), 124 (11), 123 (3), 97 (7·5), 81 (76), 80 (100), 79 (37), 69 (10), 53 (10), 41 (18), 39 (16). [2,2-$^2H_2$]-2-(3-Cyclohexenyl)ethanol (*XXXI*) was prepared from *XXX* by reduction with lithium aluminum hydride as described for *XXVI*; $n_D^{20} = 1{\cdot}4877$.

[9,9-$^2H_2$]-7-Oxabicyclo[4.3.0]nonane (*XXXII*)

Was prepared from *XXXI* as described for *XXVII*. Yield 78%, $n_D^{20} = 1{\cdot}4662$; ^{1}H NMR spectrum: 3·96 (dm, $J_d = 8{\cdot}0$ Hz, $J_m \leqq 0{\cdot}8$ Hz, 1 H), 3·80 (dm, $J_d = 8{\cdot}0$ Hz, 1 H), 3·81 (ddd, $J = 3{\cdot}9$ Hz, 1 H), 2·00 (m, 2 H), 1·57 (m, 3 H, 1·45 (m, 2 H), 1·25 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 128 (17), 127 (6·5), 126 (0·7), 99 (3), 85 (100), 84 (15), 72 (3·5), 67 (4), 57 (11). Deuterium content: 84·5% $^2H_2$, 15% $^2H_1$, 0·5% $^2H_0$.

[2-^{2}H)-2-(2-Benzyloxyethyl)cyclohexanone (*XXXIII*)

Alcohol *XXII* (1·08 g, 4·6 mmol) in dichloromethane (20 ml) was oxidized with pyridinium chlorochromate (2·6 g, 12 mmol) at 20°C for 4 h. After a standard workup[7] it was obtained 1·02 g (96%) of *XXXIII*. Mass spectrum (*m/z*, rel. intensity): 233 (1), 205 (2), 189 (6), 142 (10), 126 (12), 124 (12), 99 (53), 98 (16), 91 (100), 83 (11), 71 (12), 65 (14), 56 (13), 55 (11), 41 (12).

cis-[2-^{2}H]-2-(2-Benzyloxyethyl)cyclohexanol (*XXXIV*)

A solution of lithium tri-s-butyl borohydride[10] in tetrahydrofuran (10 ml, 10 mmol) was added dropwise under argon at −60°C to the ketone *XXXIII* (980 mg, 4·2 mmol) in tetrahydrofuran (3 ml). After 1 h stirring at −60°C and 12 h at −5°C the excessive hydride was decomposed with water and the borane was oxidized with hydrogen peroxide[10]. Ether (30 ml) was added and the solution was worked up to yield 1·02 g (97%) of *XXXIV*. ^{1}H NMR spectrum: 7·30 (s, 5 H), 4·51 (s, 2 H), 3·83 (m, $W = 9$ Hz, 1 H), 3·52 (m, 2 H), 2·42 (d, 1 H), 1·50 (m, 10 H); mass spectrum (*m/z*, rel. intensity): 235 (0·5), 217 (2), 144 (3), 126 (18), 111 (15), 108 (18), 107 (20), 94 (24), 91 (100), 82 (32), 45 (23), 31 (25).

cis-[2-^{2}H]-2-(2-Hydroxyethyl)cyclohexanol (*XXXV*)

Was prepared from *XXXIV* as described for *XXIII*. Yield 93%; ^{1}H NMR spectrum: 3·81 (m, $W = 8$ Hz, 1 H), 3·61 (m, 2 H), 2·89 (s, 2 H), 1·38 (m, 10 H); mass spectrum (*m/z*, rel. intensity): 145 (13), 127 (14), 126 (7), 109 (18·5), 108 (13), 101 (33), 99 (88), 83 (100), 71 (49), 70 (43), 68 (77), 67 (63), 55 (95), 41 (90), 31 (57).

cis-[1-^{2}H]-7-Oxabicyclo[4.3.0.]nonane (*XXXVI*)

Was prepared from *XXXV* as described for *V*. Yield 45%, $n_D^{20} = 1{\cdot}4662$; ^{1}H NMR spectrum: 3·96 (m, 1 H), 3·81–3·80 (m, 2 H), 2·01 (m, 1 H), 1·87 (m, 1 H), 1·58 (m, 3 H), 1·44 (m, 2 H), 1·25 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 127 (23), 126 (6·5), 97 (4), 84 (8), 83 (100), 68 (5·5), 67 (5), 56 (11), 55 (12·5). Deuterium content: 92% $^2H_1$, 8% $^2H_0$.

trans,cis-2-(3-Hydroxypropyl)cyclohexanols *XL*, *XLVI*

A mixture of lactones *XXXVIII* (11·6 g, 75·4 mmol) in ether (50 ml) was reduced with lithium aluminum hydride (2 g, 53 mmol) while refluxing for 30 min. The excessive hydride was decomposed with a sodium sulphate solution and the ethereal solution was worked up. Yield 11·1 g (93%) of a mixture of *XL* and *XLVI*. The mixture (7·1 g, 45 mmol) in pyridine (40 ml) was treated with benzoyl chloride (6·4 g, 45·6 mmol) at −30°C for 4 h. Ether (100 ml) was added and the ethereal solution was worked up. The mixture of benzoates *XLI* and *XLVII* was separated on a silica gel column (elution with a mixture of light petroleum and ether, 3 : 2) to yield 4·5 g of the *cis*-isomer *XLVII* (higher R_F-value) and 3·3 g of the *trans*-isomer *XLI*. *XLVII*: For $C_{16}H_{22}O_3$ (262·3) calculated: 73·25% C, 8·45% H; found: 73·41% C, 8·53% H. ^{1}H NMR spectrum: 8·04 (m, 2 H), 7·40 7·59 (m, 3 H), 4·33 (t, J = 6·4 Hz, 2 H), 3·89 (m, W = 14 Hz, 1 H), 2·29 (s, 1 H), 1·38—2·00 (m, 9 H), 1·27 (m, 4 H). *XLI*: For $C_{16}H_{22}O_3$ (262·3) calculated: 73·25% C, 8·45% H; found: 73·08% C, 8·31 % H; ^{1}H NMR spectrum: 8·05 (m, 2 H), 7·40—7·59 (m, 3 H), 4·34 (t, J = 7·4 Hz, 2 H), 3·23 (ddd, J = 9·0, 9·0 and 4·6 Hz, 1 H), 1·92 (m, 4 H), 1·70 (m, 4 H), 1·27 (m, 6 H). The benzoates *XLI* and *XLVII* were hydrolyzed as described for *XII* to furnish diols *XL* and *XLVI*, respectively, in 90—95% yield. *XL*: For $C_9H_{18}O_2$ (158·2) calculated: 68·31% C, 11·47% H; found: 68·16% C, 11·55% H; ^{1}H NMR spectrum: 3·67 (t, J = 6·2 Hz, 2 H), 3·26 (dd d, J = 9·4, 9·4 anp 4·6 Hz, 1 H), 2·56 (m, 2 H), 1·99 (m, 1 H), 1·80 (m, 5 H), 1·55 (m, 1 H), 1·28 (m, 5 H), 1·00 (m, 1 H). *XLVI*: For $C_9H_{18}O_2$ (158·2) calculated: 68·31% C, 11·47% H; found: 68·55% C, 11·42% H; ^{1}H NMR spectrum: 3·90 (m, W = 8 Hz, 1 H), 3·65 (ddd, J = 6·2, 6·2 and 2·0 Hz, 2 H), 1·98 (s, 2 H), 1·81 (m, 1 H), 1·44—1·71 (m, 10 H), 1·35 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 158 (6), 140 (14), 122 (23), 115 (15), 111 (30), 107 (15), 97 (68), 96 (49), 81 (74), 79 (57), 68 (57), 67 (82), 57 (68), 55 (89), 41 (100), 31 (37).

trans-2-Oxabicyclo[4.4.0]decane (*XLIV*)

Was prepared from *XLI* as described for *V*. Yield 51%, n_D^{20} = 1·4708 (ref.[4] gives n_D^{20} = 1·4716 for a mixture of *cis* and *trans* isomers); ^{1}H NMR spectrum: 3·97 (dddd, J = 11·5, 4·6, 1·7 and 1·7 Hz, 1 H), 3·44 (ddd, J = 11·5, 11·5 and 30 Hz, 1 H), 2·89 (m, W = 23 Hz, 1 H), 1·51—1·90 (m, 7 H), 1·12—1·36 (m, 6 H); mass spectrum (*m/z*, rel. intensity): 140 (23), 139 (3·5), 98 (7), 97 (100), 83 (4), 81 (5), 79 (9), 69 (10), 67 (12), 55 (10), 43 (5), 41 (18·5), 30 (5).

cis-2-Oxabicyclo[4.4.0]decane (*L*)

Was prepared from *XLVI* as described for *V*. Yield 55%, b.p. 85°C/6·7 kPa, n_D^{20} = 1·4749; ^{1}H NMR spectrum: 3·98 (m, W = 19 Hz, 1 H), 3·45 (ddd, J = 11·6, 11·6 and 2·7 Hz, 1 H), 3·54 (ddd, J = 3·0, 3·0 and 3·0 Hz, 1 H), 1·78 (m, 5 H), 1·60 (m, 2 H), 1·46 (m, 3 H), 1·30 (m, 3 H); mass spectrum (*m/z*, rel. intensity): 140 (23·5), 139 (2·5), 98 (7), 97 (100), 83 (4), 81 (5), 79 (8), 69 (9), 67 (10), 55 (10·5), 43 (5·5), 41 (18·5), 30 (5·5).

trans,cis-2-([3,3-$^2H_2$]-3-Hydroxypropyl)cyclohexanols (*XLII* and *XLVIII*)

Were prepared from *XXXVIII* and separated as described for *XL*. *XLII*: b.p. 105—108°C/13 Pa; ^{1}H NMR spectrum: 3·22 (ddd, J = 9·5, 9·5 and 4·6 Hz, 1 H), 2·02 to 1·94 (m, 3 H), 1·74 (m, 5 H), 1·48 (m, 1 H), 1·20 (m, 5 H), 0·96 (m, 1 H). *XLVIII*: b.p. 105°C/13 Pa; ^{1}H NMR spectrum 3·89: (m, W = 8 Hz, 1 H), 1·44—1·90 (m, 13 H), 1·35 (m, 2 H).

trans-[3,3-$^2H_2$]-2-Oxabicyclo[4.4.0]decane (*XLV*)

Was prepared from *XLII* as described for *V*. Yield 48%, n_D^{20} = 1·4688; ^{1}H NMR spectrum: 2·89 (m, *W* = 23 Hz, 1 H), 1·90 (m, 1 H), 1·68 (m, 6 H), 1·31 (m, 6 H); mass spectrum (*m/z*, rel. intensity): 142 (23·5), 141 (4·6, 140 (0·2), 99 (100), 98 (8), 85 (3·5), 81 (6), 71 (5), 69 (6), 67 (10), 55 (5·5), 54 (5), 43 (5), 42 (6), 41 (12). Deuterium content: 95% $^2H_2$, 4·5% $^2H_1$, 0·5% $^2H_0$.

cis-[3,3-$^2H_2$]-2-Oxabicyclo[4.4.0]decane (*LI*)

Was prepared from *XLVIII* as described for *V*. Yield 50%, n_D^{20} = 1·4743; ^{1}H NMR spectrum: 3·54 (m, *W* = 8·5 Hz, 1 H), 1·71 (m, 7 H), 1·47 (m, 3 H), 1·30 (m, 3 H); mass spectrum (*m/z*, rel. intensity): 142 (23), 141 (4), 140 (0·3), 99 (100), 98 (8), 85 (4), 81 (7), 71 (6), 69 (4·5), 67 (8), 55 (7), 43 (5·5), 42 (6), 41 (11·5). Deuterium content: 94·5% $^2H_2$, 5% $^2H_1$, 0·5% $^2H_0$.

cis,trans-[1-^{2}H]-2-Oxabicyclo[4.4.0]-3-decanone (*XXXIX*)

3-(2-Oxocyclohexyl)propannitrile (ref.[8], 1·2 g, 7·9 mmol) in methanol (10 ml) was added at 0°C to a solution of sodium borodeuteride (160 mg, 3·8 mmol) in methanol (5 ml). After 2 h at 0°C ether was added, the mixture was poured into water and the ethereal solution worked up. Distillation gave a mixture of 3-(2-hydroxycyclohexyl)propannitriles (1·05 g, 86%), b.p. 115–120°C/1·7 kPa (ref.[8] gives b.p. 141–145°C/1·3 kPa for the non-labelled compound); IR spectrum (cm^{-1}): 3 470, 2 268, 2 140, 1 469, 1 440, 1 270, 1 160, 1 100, 1 000, 952, 760. The nitriles were added to a solution of sodium hydroxide (1 g) and triethylbenzylammonium chloride (100 mg) in ethanol (2 ml) and water (10 ml) and the mixture was refluxed for 6 h. After acidification were the lactones *XXXIX* extracted with chloroform and the extract was worked up. Distillation gave 880 mg (72% O of *XXXIX*; IR spectrum (cm^{-1}): 2 175, 1 750, 1 450, 1 345, 1 290, 1 257, 1 220, 1 142, 1 128, 1 072, 1 005, 980; mass spectrum (*m/z*, rel. intensity): 155 (9), 137 (4), 127 (5), 112 (19), 111 (33), 99 (34), 83 (81), 82 (88), 69 (71), 68 (100), 67 (88), 55 (56), 41 (74), 39 (50).

trans,cis-[1-^{2}H]-2-(3-Hydroxypropyl)cyclohexanols (*LII* and *LV*, respectively)

Were prepared from *XXXIX* as described for *XL*. *LII*: ^{1}H NMR spectrum: 3·67 (t, *J* = 6·2 Hz, 2 H), 2·41 (broad s, 2 H), 1·99 (m, 1 H), 1·80 (m, 5 H), 1·58 (m, 1 H), 1·30 (m, 5 H), 1·02 (m, 1 H). *LV*: ^{1}H NMR spectrum: 3·65 (m, 2 H), 1·88 (s, 2 H), 1·81 (m, 1 H), 1·45–1·70 (m, 10 H), 1·37 (m, 2 H).

trans-[1-^{2}H]-2-Oxabicyclo[4.4.0]decane (*LIV*)

Was prepared from *LII* as described for *V*, n_D^{20} = 1·4694;; ^{1}H NMR spectrum: 3·97 (dddd, *J* = 11·5, 4·6, 1·7 and 1·7 Hz, 1 H), 3·44 (ddd, *J* = 11·5, 11·5 and 3·0 Hz, 1 H), 1·60–1·90 (m, 7 H), 1·18–1·45 (m, 6 H); mass spectrum (*m/z*, rel. intensity): 141 (22), 140 (3), 139 (2), 99 (7·5), 98 (100), 97 (11), 84 (4), 82 (4), 80 (5), 70 (7), 68 (7), 67 (7·5), 55 (8), 43 (5), 42 (7), 41 (12). Deuterium content: 95% $^2H_1$, 5% $^2H_0$.

cis-[1-^{2}H]-2-Oxabicyclo[4.4.0]decane (*LVII*)

Was prepared from *LV* as described for *V*, n_D^{20} = 1·4747; ^{1}H NMR spectrum: 3·98 (m, *W* = = 19 Hz, 1 H), 3·45 (ddd, *J* = 11·6, 11·6 and 2·8 Hz, 1 H), 1·57–1·88 (m, 7 H), 1·46 (m, 3 H), 1·30 (m, 3 H); mass spectrum (*m/z*, rel. intensity): 141 (22·5), 140 (2·5), 139 (1·5), 99 (7·5), 98 (100),

97 (11), 84 (4), 82 (5), 80 (6), 70 (6), 68 (6), 67 (7), 55 (8·5), 42 (6·5), 41 (12). Deuterium content: 95% $^2H_1$, 5% $^2H_0$.

1-(3-Benzoyloxypropyl)cyclohexene (*LIX*)

cis-Benzoate *XLVI* (2 g, 11·4 mmol) in pyridine (5 ml) and benzene (10 ml) was treated with *p*-toluenesulphonyl chloride (2·4 g, 12·5 mmol) at room temperature. After 72 g standing the mixture was poured into water, the product extracted with chloroform and worked up. The tosylate *LVIII* (4·5 g, m.p. 65–67°C) was dissolved in dioxane (15 ml) and treated with 1,8-diazabicyclo[5.4.0]-7-undecene (2·5 g) while refluxing under argon for 3 h. After cooling light petroleum (50 ml) was added, the mixture was poured into water and the organic phase was worked up. Yield 2·45 g (93%); for $C_{16}H_{20}O_2$ (244·3) calculated: 78·65% C, 8·25% H; found: 79·11% C, 8·13% H. ^{1}H NMR spectrum: 8·05 (m, 2 H), 7·41–7·59 (m, 3 H), 5·45 (m, 1 H), 4·31 (t, J = = 6·5 Hz, 2 H), 2·07 (m, 2 H), 1·80–1·97 (m, 5 H), 1·59 (m, 5 H).

trans-[2-^{2}H]-2-(3-Benzyloxypropyl)cyclohexanol (*LXII*)

Benzoate *LIX* (2·4 g, 9·8 mmol) was hydrolyzed as described for *XLI*. The resulting alcohol *LX* (yield 1·8 g, b.p. 120°C/2 kPa) was treated with benzyl bromide as described for *XIX*. The benzyl ether obtained (*LXI*, yield 1·8 g, b.p. 110°C/13 Pa) was deuterioborated as described for *XXII* to yield 1·92 g (99%) of *LXII*. ^{1}H NMR spectrum: 7·34 (m, 5 H), 4·46 (s, 2 H), 3·44 (t, J = 6·0Hz, 2 H), 3·18 (ddd, J = 9·7, 4·8 and 1·2 Hz, 1 H), 1·91 (m, 1 H), 1·72 (m, 5 H), 1·57 (m, 2 H), 1·19 (m, 5 H): mass spectrum (*m/z*, rel. intensity): 249 (0·4), 231 (1), 213 (0·7), 158 (1·6), 140 (15), 139 (7), 123 (10), 122 (27), 121 (15), 107 (13), 91 (100), 79 (13), 67 (14), 55 (11), 41 (12).

trans-[2-^{2}H]-2-(3-Hydroxypropyl)cyclohexanol (*LXIII*)

Was prepared from *LXII* as described for *XXIII*. ^{1}H NMR spectrum: 3·67 (t, J = 6·2 Hz, 2 H), 3·27 (ddd, J = 9·4, 4·6 and 1·1 Hz, 1 H), 2·48 (m, 2 H), 1·99 (m, 1 H), 1·80 (m, 4 H), 1·55 (m, 1 H), 1·28 (m, 5 H), 1·00 (m, 1 H).

trans-[6-^{2}H]-2-Oxabicyclo[4.4.0]decane (*LXIV*)

Was prepared from *LXIII* as described for *V*. Yield: 52%, n_D^{20} = 1·4696; ^{1}H NMR spectrum: 3·97 (dddd, J = 11·5, 4·6, 1·7 and 1·7 Hz, 1 H), 3·44 (ddd, J = 11·5, 11·5 and 3·0 Hz, 1 H), 2·88 (m, W = 16 Hz, 1 H), 1·51–1·90 (m, 6 H); mass spectrum (*m/z*, rel. intensity): 141 (22), 140 (4·4), 98 (9), 97 (100), 83 (3), 82 (4), 79 (5·5), 69 (8), 67 (7·5), 55 (9), 41 (13). Deuterium content: 98% $^2H_1$, 2% $^2H_0$.

cis-[2-^{2}H]-2-(3-Benzyloxypropyl)cyclohexanol (*LXVI*)

Alcohol *LXII* (1 g, 4 mmol) in dichloromethane (20 ml) was treated with pyridinium chlorochromate (2 g, 9·3 mmol) for 1 h. After standard work-up[7] the crude ketone *LXV* (a single spot in thin layer chromatography) was reduced with lithium tri-s-butyl borohydride as decribed for *XXXIV*. Yield 630 mg (63%) of *LXVI*; ^{1}H NMR spectrum: 3·90 (m, W = 6 Hz), 1 H), 3·65 (m, 2 H), 1·98 (s, 2 H), 1·81 (m, 1 H), 1·44–1·71 (m, 9 H), 1·35 (m, 2 H); mass spectrum (*m/z*, rel. intensity): 249 (0·5), 231 (1), 213 (0·6), 158 (7·4), 140 (17), 139 (8), 123 (11), 122 (28, 121 (15), 107 (12). 91 (100), 79 (17), 67 (14), 65 (11), 55 (13), 41 (18).

cis-[6-^{2}H]-2-Oxabicyclo[4.4.0]decane (*LXVII*)

Benzyl ether *LXVI* (600 mg) was hydrogenated on palladium (100 mg) in ethanol (10 ml) as described for *XXIII*. The *cis*-diol *LXVII* obtained (yield 93%, b.p. 103°C/9 Pa) was cyclized as described for *V* to produce the ther *LXVIII* in 49% yield. $n_D^{20} = 1{\cdot}4741$; ^{1}H NMR spectrum: 3·98 (m, $W = 19$ Hz, 1 H), 3·54 (m, $W = 7{\cdot}5$ Hz, 1 H), 3·45 (ddd, $J = 11{\cdot}6$, 11·6 and 2·7 Hz, 1 H), 1·78 (m, 4 H), 1·60 (m, 2 H), 1·46 (m, 3 H), 1·30 (m, 3 H); mass spectrum (*m*/*z*, rel. intensity): 141 (22), 140 (4·5), 98 (8), 97 (100), 82 (4·5), 79 (6), 69 (8), 68 (6·5), 67 (6), 55 (8), 41 (11). Deuterium content: 91% $^2H_1$, 9% $^2H_0$.

3-(3-Cyclohexenyl)propannitrile (*XXII*)

Alcohol *XXV* (2·5 g, 19·8 mmol) in pyridine (5 ml) was treated with *p*-toluenesulphonyl chloride (4 g), and the mixture was allowed to stand at 0°C for 20 h. The mixture was poured into water, the product extracted with chloroform and worked up. The crude tosylate *XLIX* (oil, 5·2 g, 94%) was dissolved in dimethyl sulphoxide (10 ml) and treated with sodium cyanide (2 g) at 100°C for 2 h. The mixture was poured into water, the nitrile *LXXII* was extracted with light petroleum and worked up. Distillation gave 2·3 g (90%) of *LXXII*, b.p. 110°C/2 kPa, $n_D^{20} = 1{\cdot}4788$. For $C_9H_{13}N$ (135·2) calculated: 79·95% C, 9·69% H; found: 80·23% C, 9·44% H. IR spectrum (cm^{-1}): 3 035, 2 260, 1 664, 730.

[2,2-$^2H_2$]-3-(3-Cyclohexenyl)propannitrile (*LXXVI*)

Was prepared from *XXVI* as described for *LXXII*. $n_D^{20} = 1{\cdot}4784$; mass spectrum (*m*/*z*, mass spectrum (*m*/*z*, rel. intensity): 137 (27), 136 (24), 122 (7), 120 (5), 119 (7), 109 (6), 95 (62), 94 (64), 81 (100), 79 (61), 67 (51); IR spectrum (cm^{-1}): 3 035, 2 270, 1 665, 875, 730.

[3,3-$^2H_2$]-3-(3-Cyclohexenyl)propannitrile (*LXXX*)

Was prepared from *XXXI* as described for *LXXII*. $n_D^{20} = 1{\cdot}4788$; mass spectrum (*m*/*z*, rel. intensity): 137 (21), 136 (21), 122 (6), 119 (4), 118 (4), 109 (5), 97 (37), 96 (50), 81 (100), 79 (33), 69 (32); IR spectrum (cm^{-1}): 3 036, 2 250, 2 120, 1 664, 1 320, 945, 730.

3-(3-Cyclohexenyl)propionic Acid (*LXXIII*)

A mixture of nitrile *LXXII* (1 g), sodium hydroxide (1 g) and triethylbenzylammonium chloride (100 mg) in water (10 ml) was refluxed for 7 h. After acidification the product was extracted with chloroform and worked up. Distillation gave 1·05 g (92%) of *LXXIII*, b.p. 140–142°C/1·7 kPa, $n_D^{20} = 1{\cdot}4819$ (ref.[12] gives $n_D^{25} = 1{\cdot}4803$ for the non-labelled derivative).

[2,2-$^2H_2$]-3-(3-Cyclohexenyl)propionic Acid (*LXXVII*)

Was prepared from *LXXVI* as described for *LXXIII*, but using sodium deuteroxide and heavy water for the hydrolysis. Yield 91%, $n_D^{20} = 1{\cdot}4820$; mass spectrum (*m*/*z*, rel. intensity): 156 (8·5), 138 (27), 120 (3), 110 (11), 95 (43·5), 94 (100), 81 (17), 79 (88), 76 (19).

3,3-$^2H_2$]-3-(3-Cyclohexenyl)propionic Acid (*LXXXI*)

Was prepared from *LXXX* as described for *LXXIII*. $n_D^{20} = 1{\cdot}4822$; mass spectrum (*m*/*z*, rel. intensity): 156 (11·5), 138 (21), 137 (12), 120 (2), 119 (2), 110 (8), 109 (7), 97 (36), 96 (97), 95 (43), 81 (100), 79 (57), 67 (13).

[3-(3-Cyclohexenyl)propanol (*LXXIV*)

Acid *LXXIII* (1 g, 6·5 mmol) was reduced with lithium aluminum hydride (300 mg, 8 mmol) in ether (30 ml) under standard conditions. Work-up afforded 850 mg (93%) of *LXXIV*, b.p. 110°C/1·7 kPa, $n_D^{20} = 1{\cdot}4835$ (ref.[17] gives b.p. 115–119°C/2·3 kPa, $n_D^{21} = 1{\cdot}4830$).

[2,2-$^2H_2$]-3-(3-Cyclohexenyl)propanol (*LXXVIII*)

Was prepared from *LXXVII* as described for *LXXIV*. Yield 90%, $n_D^{20} = 1{\cdot}4835$; mass spectrum (*m/z*, rel. intensity): 142 (10), 124 (12), 111 (6), 109 (8), 108 (10), 96 (33), 95 (17), 94 (56), 81 (100), 79 (67), 67 (24).

[3,3-$^2H_2$]-3-(3-Cyclohexenyl)propanol (*LXXXII*)

Was prepared from *LXXXI* as described for *LXXIV*. Yield 90%, $n_D^{20} = 1{\cdot}4830$; mass spectrum (*m/z*, rel. intensity): 142 (11), 141 (2·5), 124 (7), 123 (6), 109 (10), 108 (10), 96 (48), 81 (100), 80 (40), 79 (56), 67 (20).

cis-[10-^{2}H]-2-Oxabicyclo[4.4.0]decane (*LXXV*)

Was prepared from *LXXIV* as described for *XXVIII*. Yield 83%, $n_D^{20} = 1{\cdot}4754$; mass spectrum (*m/z*, rel. intensity): 141 (22), 140 (4·5), 98 (7·5), 97 (100), 83 (5), 79 (5·5), 69 (7·5), 68 (6), 67 (5·5), 55 (9), 43 (5). Deuterium content: 91% $^2H_1$, 9% $^2H_0$.

cis-[4,4-$^2H_2$]-2-Oxabicyclo[4.4.0]decane (*LXXIX*)

Was prepared from *LXXVIII* as described for *XXVII*. Yield 76%, $n_D^{20} = 1{\cdot}4748$; mass spectrum (*m/z*, rel. intensity): 142 (27), 141 (3), 100 (7·5), 99 (100), 85 (3·5), 81 (7), 71 (6), 69 (4), 67 (4), 57 (4), 55 (5·5), 41 (8). Deuterium content: 96% $^2H_2$, 3·5% $^2H_1$, 0·5% $^2H_0$.

cis-[5,5-$^2H_2$]-2-Oxabicyclo[4.4.0]decane (*LXXXIII*)

Was prepared from *LXXXII* as described for *XXVII*. Yield 70%, $n_D^{20} = 1{\cdot}4745$; mass spectrum (*m/z*, rel. intensity): 142 (23), 141 (7), 140 (0·8), 99 (100), 98 (21), 97 (3), 81 (7·5), 80 (4), 71 (6), 69 (5·5), 67 (7), 57 (5), 56 (5·5), 55 (6·5). Deuterium content: 81% $^2H_2$, 16% $^2H_1$, 3% $^2H_0$.

The author is grateful to Professor A. Vystrčil for the permission to carry out the syntheses in Department of Organic Chemistry, Charles University, Prague. Thanks are also due to Dr V. Hanuš for his over-all support.

REFERENCES

1. Cantor S. E., Tarbell D. S.: J. Amer. Chem. Soc. *86*, 2902 (1964).
2. Yamamoto Y., Gargiulo R. J., Tarbell D. S.: J. Org. Chem. *36*, 846 (1971).
3. Clive D. L. J., Chittattu G., Wong C. K.: Can. J. Chem. *55*, 3894 (1977).
4. Benneville P. L., Connor R.: J. Amer. Chem. Soc. *62*, 283 (1940).
5. Spéziale V., Amat M., Lattes A.: J. Heterocycl. Chem. *13*, 349 (1976).
6. Newman M. S., Vander Werf C. A.: J. Amer. Chem. Soc. *67*, 233 (1945).
7. Corey E. J., Suggs J. W.: Tetrahedron Lett. *1975*, 2647.

8. Stork G., Brizzolara A., Landesman H. K., Szmuszkovicz J., Terrell R.: J. Amer. Chem. Soc. *85*, 207 (1963).
9. House H. O., Babad H., Toothill R. B., Noltes A. W.: J. Org. Chem. *27*, 4141 (1962).
10. Brown H. C., Krishnamurthy S.: J. Amer. Chem. Soc. *94*, 7159 (1972).
11. Youssef A., A, Sharaf S. M.: J. Org. Chem. *33*, 2581 (1968).
12. House H. O., Carlson R. G., Babad H.: J. Org. Chem. *28*, 3359 (1963).
13. Kuivila H. G.: Synthesis *1970*, 499.
14. Klein J.: J. Amer. Chem. Soc. *81*, 3611 (1959).
15. Brown H. C.: *Organic Syntheses* vis *Boranes*. Wiley, New York 1974.
16. Vierhapper F. W., Eliel E. L.: J. Org. Chem. *42*, 51 (1977).
17. Julia M., Surzur J. M., Latz L., LeGoffic F.: Bull. Soc. Chim. Fr. *1964*, 1116.

Translated by the author.