Tetrahedron. Vol. 28, pp. 3475 to 3484. Pergamon Press 1972 Printed in Great Britain

STEREOCHEMICAL STUDIES—XIII[1]

CYCLIC AMINOALCOHOLS AND RELATED COMPOUNDS—VI[1] SYNTHESIS OF THE FOUR 2-AMINO-4-*t*-BUTYLCYCLOPENTANOL ISOMERS

G. BERNÁTH *

Institute of Organic Chemistry, A. József University Szeged, Hungary

and

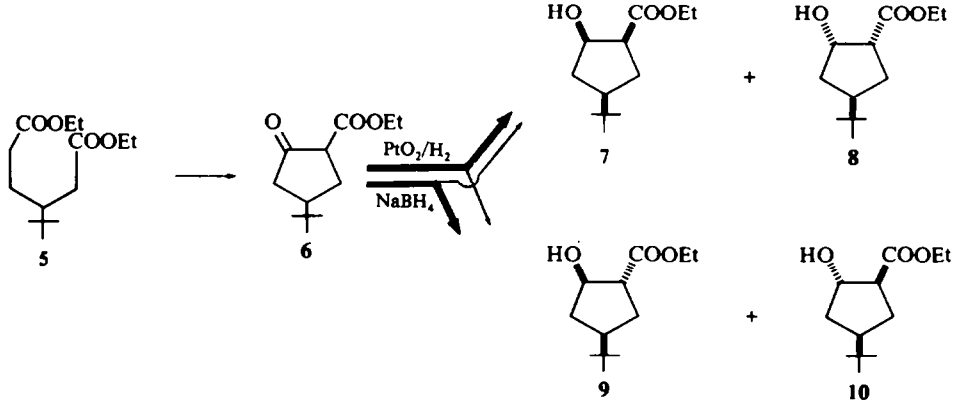
M. SVOBODA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Prague, Czechoslovakia

(*Received in the UK* 7 *February* 1972; *Accepted for publication* 8 *March* 1972)

Abstract—From diethyl 3-t-butyladipate (**5**), *via cis*- and *trans*-4-t-butylcyclopentene-1,2-oxide (**31, 32**) as key compounds, the syntheses of *cis*-2-amino-*cis*-4-t-butylcyclopentanol (**1**), *cis*-2-amino-*trans*-4-t-butylcyclopentanol (**2**), *trans*-2-amino-*cis*-4-t-butylcyclopentanol (**3**) and *trans*-2-amino-*trans*-4-t-butylcyclopentanol (**4**) have been achieved. **1**, **3** and **4** were also synthesized from the corresponding 2-hydroxy-4-t-butylcarboxylic acids by Curtius degradation of the hydrazides (**11**, **18**, **19**). The steric course of process leading to the above compounds is discussed.

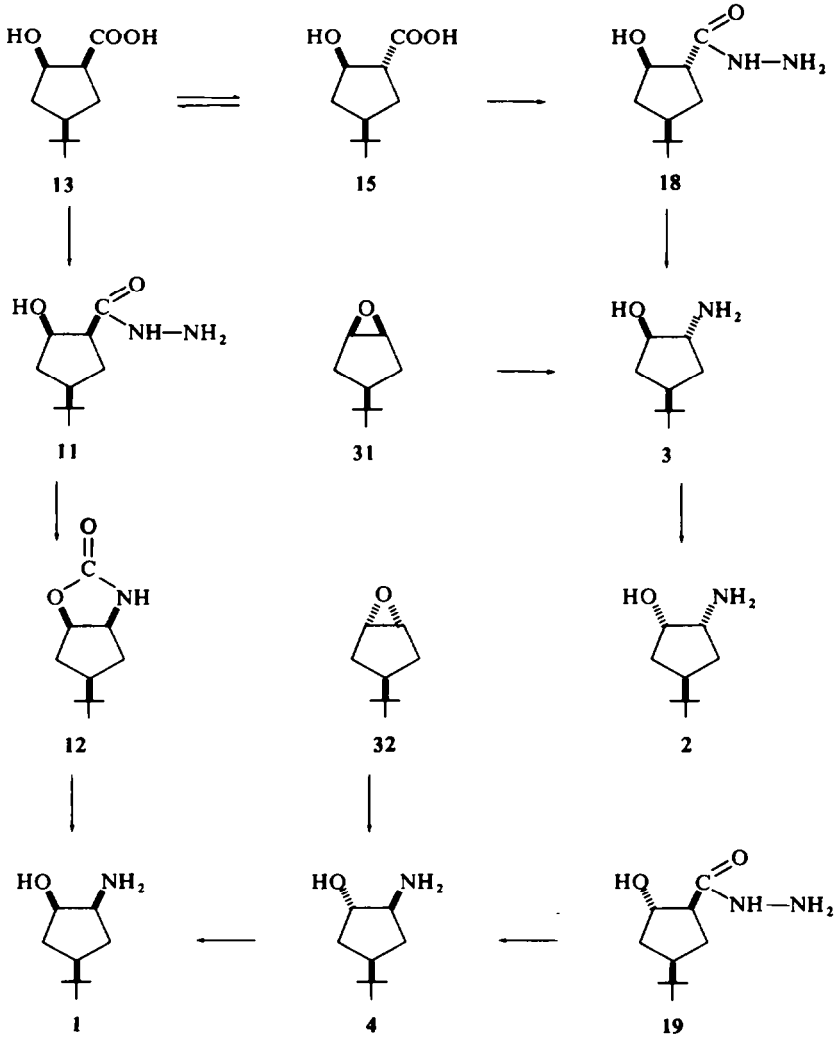
IN CONTRAST to intensive investigations[2-4] with t-butylcyclohexane derivatives furnishing valuable information on the conformation of the cyclohexane skeleton, t-butylcyclopentane derivatives have been little studied.[5-7] Our aim was to study the stereospecific reactions and spectroscopic properties of t-butylcyclopentane derivatives, comparing them with related cyclohexane analogues, *e.g.* 2-amino-4-t-butylcyclohexanols,[4] in the hope of obtaining data for conformational relationships in the cyclopentane skeleton. This paper reports the synthesis of the four isomeric 2-amino-



SCHEME 1

* Author to whom correspondence should be addressed.

4-t-butylcyclopentanols (**1–4**), the model compounds of these investigations. 2-Carbethoxy-4-t-butylcyclopentanone (**6**),[6] prepared by Dickmann cyclization of **5**, was used as common starting material. Hydrogenation of **6** in the presence of PtO_2 catalyst yielded *cis*-2-carbethoxy-*cis*-4-t-butylcyclopentanol (**7**) as main product, with a small amount of **8**. The quantity of the "1,2-*trans*" isomers (**9–10**) was 32·6%. The mixture of **7** and **8** could be separated from the mixture of **9** and **10** by fractional distillation on a column of 30 theoretical plates. Redistilling the **7** and **8** mixture gave only **7** of higher b.p. in a stereohomogeneous form, which gave, *via* hydrazide **11** and hydrolysis of the cyclic urethane **12**, *cis*-2-amino-*cis*-4-t-butyl cyclopentanol (**1**), also synthesized in an independent way.



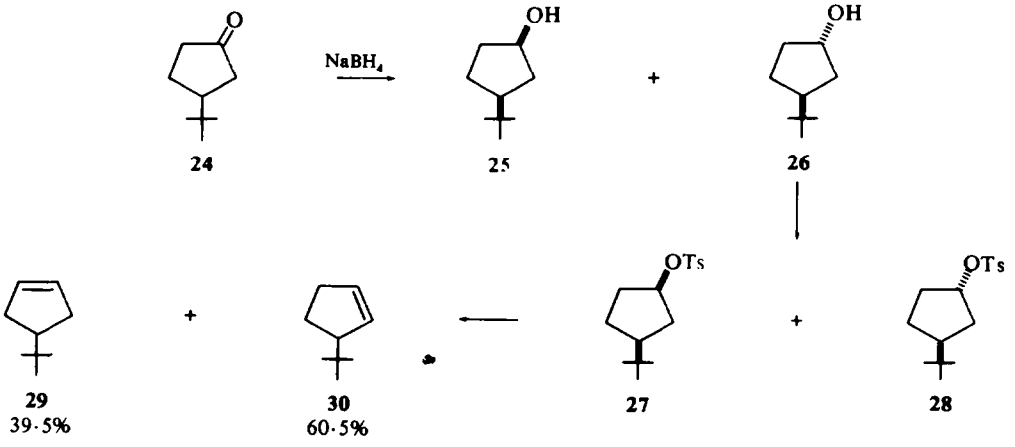
SCHEME 2

For the synthesis of **1**, it is not necessary to start with stereohomogeneous **7**. The different solubilities of the *cis* carboxylic acids (**13**, **14**), as well as the corresponding hydrazides, permit the separation of the all-*cis* isomers (**13**, **11**). Unfortunately, the *trans* esters (**9**, **10**) could not be completely separated either by distillation or by gas chromatography; therefore pure **8**, **9** and **10** remained equally unavailable for the synthesis of **2**, **3** and **4**, respectively. We attempted the preparation of these aminoalcohols in different ways. The independent synthetic routes and the interconversions of the aminoalcohols allowed us to deduce the configurations of all four isomers.

Equilibration of **13** with 40% KOH and subsequent fractional distillation gave stereohomogeneous *trans*-2-hydroxy-*trans*-4-t-butylcyclopentanecarboxylic acid (**15**). The isomerization was followed by gas chromatographic analysis of the methyl esters. Interestingly, no dehydration was observed during the isomerization, whereas 2-hydroxycyclopentanecarboxylic acid give 1-cyclopentene-1-carboxylic acid under similar conditions. From **15**, *via* **18**, *trans*-2-amino-*cis*-4-t-butylcyclopentanol (**3**) was obtained.

Reduction of **6** with $NaBH_4$ was studied at different temperatures, as this process is known[8,9] to be suitable for the preparation of related cyclic ethyl *trans*-2-hydroxycarboxylates. At low temperatures the quantity of the *trans* isomers (**9** + **10**) increased at the expense of the *cis* isomers (**7** + **8**). The yields of **9** + **10** was 46·1 and 62·3%, at room temperature and −70°, respectively. The last fractions of the distillate contained mainly **10** with a smaller amount of **9**. *Trans*-2-hydroxy-*cis*-4-t-butylcyclopentanecarboxylic acid (**16**) could not be isolated in homogeneous form; however, the stereohomogeneous hydrazide (**19**) was prepared. Curtius degradation of the latter resulted in **4**.

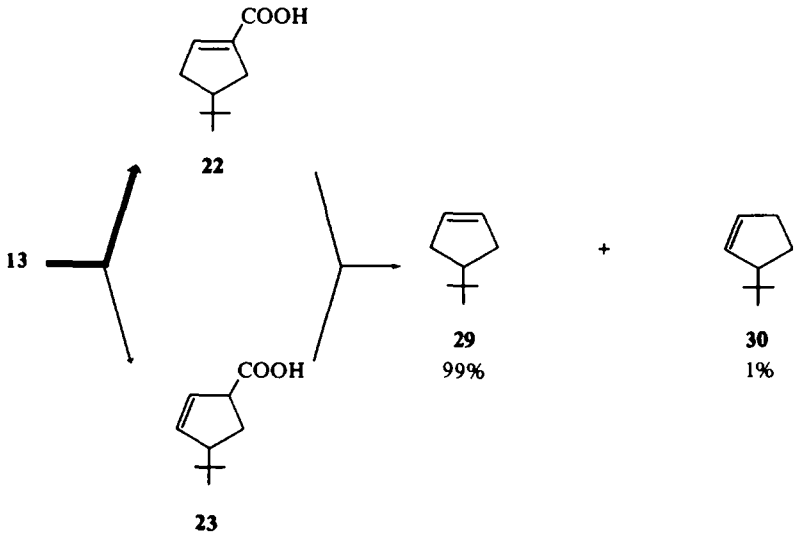
The method discussed so far yielded the *trans* aminoalcohols **3** and **4**, permitting the synthesis of the *cis* aminoalcohols **1** and **2** *via* the N-benzoyl derivatives **20** and **34** and oxazolines **21** and **35**, but for the preparation of larger quantities, a way other than Curtius degradation of the hydrazides (**18**, **19**) seemed necessary, as this synthesis, though finally yielding stereohomogeneous products, incurred considerable distillation losses, and tedious fractional crystallizations, and gave no information about the configuration of the compounds.



SCHEME 3

Another synthetic route giving better yields and also proving the stereochemistry, was elaborated starting with *cis*- and *trans*-4-t-butylcyclopentene-1,2-oxide (**31**, **32**) prepared from 4-t-butylcyclopent-1-ene (**29**).

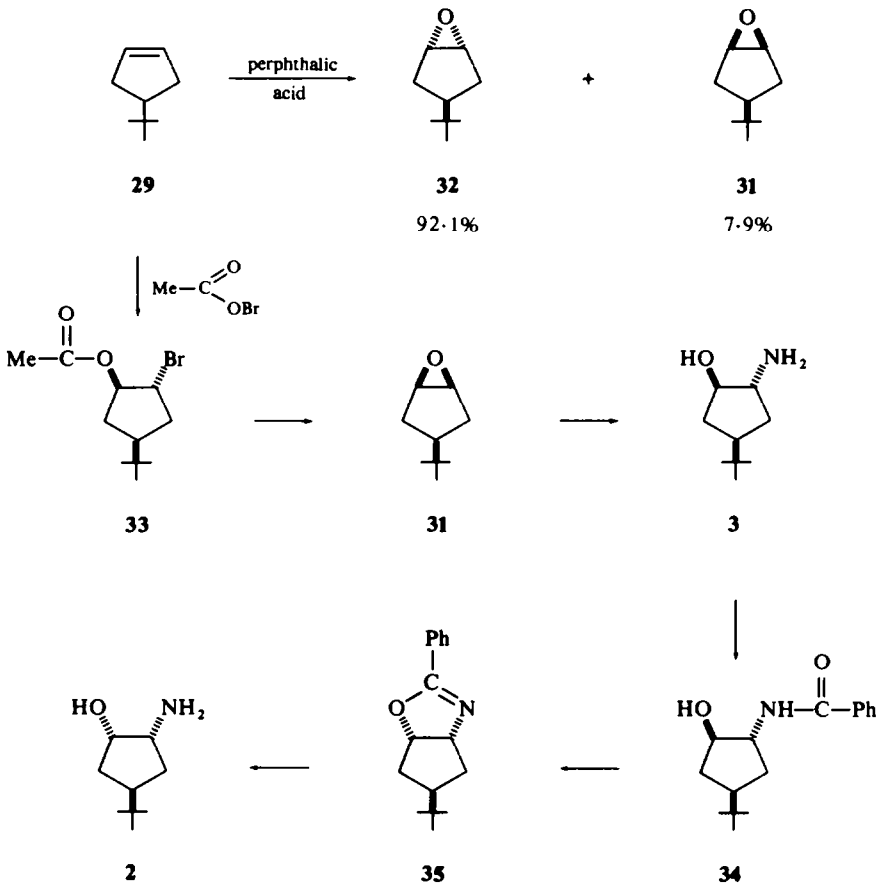
The mixture of *cis*- and *trans*-3-t-butylcyclopentanol (**25**, **26**) obtained by $NaBH_4$ reduction of 3-t-butylcyclopentanone (**24**) was converted into tosylates **27** and **28**, which, on heating in quinoline, gave a mixture of 3- and 4-t-butylcyclopent-1-ene (**29**, **30**). However, **30**, undesirable for further synthesis, was formed in 60·5% with only 39·5% of **29**. This ratio can be understood, as the $NaBH_4$ reduction of **24** gives **26** as main product. Though **29** can be separated from **30** by gas chromatography, this method does not seem suitable for larger quantities.



SCHEME 4

A practical synthesis of 4-t-butylcyclopent-1-ene (**29**) was achieved by decarboxylation of 4-t-butylcyclopent-1,2-ene-1-carboxylic acid (**22**) obtained from **13** by dehydration. When **13** was distilled at atmospheric pressure water was produced, similarly to the related 2-hydroxycarboxylic acids.[10] Decarboxylation of the olefinic acids (**22**, **23**) in quinoline with copper oxide[11] gave an olefin consisting of 99% **29** and 1% **30.** Starting from **16**, the product contained 96% of **29** and 4% of **30.**

Epoxidation of **29** with perphthalic acid resulted in 92·1% of *trans*-4-t-butylcyclopentene-1,2-oxide (**32**) in addition to *cis* isomer **31.** The isomers were easily separable by gas chromatography. Epoxidation of 4-methylcyclopent-1-ene with perlauric acid gave a 1 : 3 mixture of the *cis* and *trans* epoxides.[12, 13] The higher stereoselectivity found in our experiments obviously results from the relative steric demands of the methyl and t-butyl substituents. In the epoxidation of 4-t-butylcyclopenent-1-ene with perphthalic acid, Kauffman[7] stated formation of the *trans* epoxide to be the main reaction.



SCHEME 5

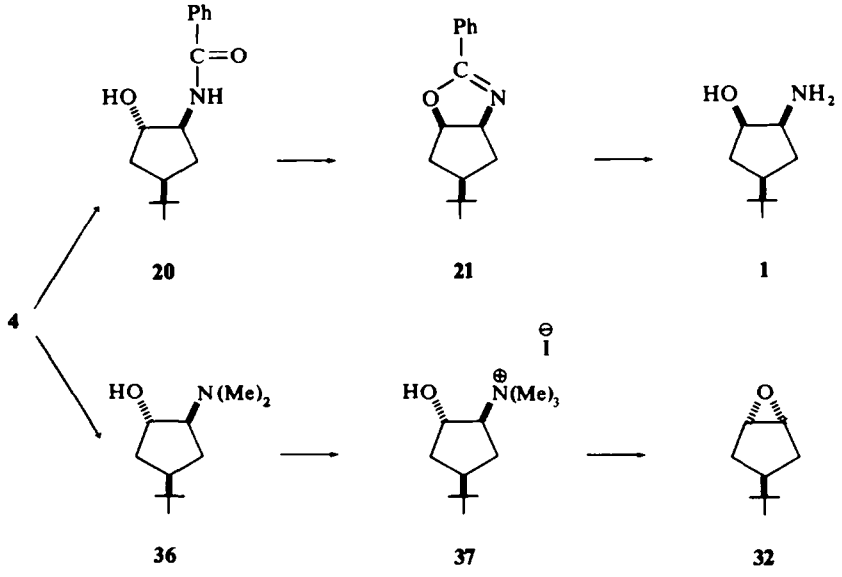
NH_4OH treatment of the epoxide mixture **32**, **32** and several recrystallizations of the aminoalcohol produced, gave stereohomogeneous **4**, identical with that prepared by the Curtius degradation of the hydrazide **19**. The preferred epoxidation *trans* to the 4-t-butyl substituent and subsequent opening of the epoxide ring to give "1,2-*trans*" configuration furnished unambiguous proof of the steric structure of **4**.

After N-benzoylation of **4**, and subjecting the N-benzoyl derivative **20** to the usual $SOCl_2$ treatment[14] *via* the oxazoline **21**, aminoalcohol **1** was obtained, identical with the product of the Curtius degradation of hydrazide **11**. The stereochemistry of **1** follows unequivocally from the above reactions. Formation of **7**, containing all three substituents in the *cis* configuration, as the main product of the catalytic reduction of **6** can be considered as additional evidence.

31 was prepared *via* the acetyl hypobromite adduct **33** formed stereospecifically from **29**. The selectivity in this case can be easily understood, as acetyl hypobromite addition even to 4-methylcyclopent-1-ene was found to be completely stereoselective.[15] Treatment

of **33** with conc KOH gave the *cis* epoxide **31** in good yield. Analogous milder processes[16] proved unsatisfactory in our case. This could be due to the steric effect of the *cis*-t-butyl group. Treatment of *cis*-4-t-butylcyclopentene-1,2-oxide with NH_4OH yielded **3**, identical with the aminoalcohol prepared *via* the hydrazide **18**.

Synthesis of the fourth isomeric aminoalcohol, *cis*-2-amino-*trans*-4-t-butylcyclopentanol (**2**), was achieved from 3 *via* the N-benzoyl derivative **34** by oxazoline (**35**) formation and subsequent hydrolysis.



SCHEME 6

Synthesis of the stereohomogeneous *trans*-epoxide was also elaborated. Preparation of the N,N-dimethyl derivative of **4**, quaternization of *trans*-2-dimethylamino-*trans*-4-t-butylcyclopentanol (**36**) with MeI and liberation of the base followed by treatment at 150° yielded stereohomogeneous **32**. The IR spectra of the *cis* and *trans* epoxides (**31**, **32**) show marked differences in the between 800–1400 cm^{-1}, while at higher wave numbers they are very similar.

The IR spectra of the aminoalcohols **1–4** and of their N,N-dimethyl derivatives were measured and numerical separation of the bands in the 3 μ region was carried out with an Elliot 503 computer using the damped least squares method. These data, together with the solvolysis reaction of the methanesulfonates of **20** and **34**, are to be reported.

EXPERIMENTAL

2-Carbethoxy-4-t-butylcyclopentanone (**6**). Diethyl 4-t-butyladipate (**5**) (88 g) was added in 1 hr to finely powdered Na (7·85 g) suspended in xylene (500 ml) at 115–120° under vigorous stirring. After heating for 4 hr, the mixture was cooled with ice and carefully treated with 10% AcOH aq (300 ml). The xylene layer has washed with water, Na_2CO_3 aq, water, dried ($MgSO_4$) and distilled to give **6** (47·8 g, 66%), b.p. 145–150°/20 mm and considerable non-volatile residue. (Found: C, 68·40; H, 9·53. $C_{12}H_{20}O_3$ requires: C, 67·89; H, 9·50%).

Catalytic reduction of 2-*carbethoxy*-4-*t-butylcyclopentanone* (**6**). **6** (129·6 g) was hydrogenated in EtOH (200 ml) in the presence of PtO_2 catalyst (2·7 g) at room temp and atm press for 11 hr. After adding fresh catalyst (2·5 g) and further shaking for 10 hr the total hydrogen uptake was 15·1 l., corresponding to the calc amount. Work-up afforded **7–10** (14·3 g, 95%). b.p. 126–138°/8 mm, consisting of 67·4% **7** + **8** and 32·6% **9** + **10**. Fractional distillation on a column of 30 theor. plates yielded **8** + **7**, then stereohomogeneous **7**, b.p. 128°/8 mm, $n_D^{20} = 1·4586$. Complete separation of the *trans* esters (**9**, **10**) could not be achieved. Fractions containing first mainly **9**, at last **9** + **10** (b.p. 134–136/8 mm, $n_D^{20} = 1·4578$) were collected.

Reduction of **6** *with* $NaBH_4$. To $NaBH_4$ (42 g, 1·11 mole) suspended in EtOH (2·5 l) at −70° bath temp **6** (300 g, 1·145 mole) in EtOH (400 ml) was added in 2 hr. The mixture was stirred at −70° for 5 hr, kept at room temp for 24 hr, and then water (500 ml) and AcOH (265 ml) added dropwise. EtOH was evaporated at 30 mm, the residue extracted with ether, the extract washed with Na_2CO_3 aq, dried ($MgSO_4$), and the ether evaporated. The product (262·4 g, 86·6%) consisted of 37·7% **7** + **8** and 62·3% **9** + **10**.

Reduction at 20° afforded (**7** + **8**):(**9** + **10**) (53·9%:46·1%). (In calculating the ratio only the combined quantity of **7–10** was taken into account, regardless of unchanged **6** (6·1%) and by-products (10·8%)).

Cis-2-*hydroxy*-cis-4-*t-butylcyclopentanecarboxylic acid* (**13**). A ~3:1 mixture of **7** + **8** (1·0 g) was shaken with 10% KOH aq for 1 hr, the solution extracted with ether, acidified with HCl and extracted with ether. This latter extract, after drying ($MgSO_4$) and evaporation, gave **13** + **14** (805 mg, 92·6%). On repeated recrystallization from benzene **13** (270 mg) m.p. 119–120°, identical with the product prepared from stereohomogeneous **7**, separated. The methyl ester was homogeneous on a capillary column of 50 m. (Found: C, 64·72; H, 9·86. $C_{10}H_{18}O_3$ requires: C, 64·49; H, 9·74%).

Cis-2-*hydroxy*-cis-4-*t-butylcyclopentanecarboxylic acid hydrazide* (**11**). Prepared from **7**, or from the above methyl ester, white, glittering plates, m.p. 196–197° (EtOH). (Found: C, 60·23; H, 10·12; N, 14·09. $C_{10}H_{20}O_2N_2$ requires: C, 59·97; H, 10·06; N, 13·99%).

Cyclic urethane (**12**) *from* cis-2-*hydroxy*-cis-4-*t-butylcyclopentanecarboxylic acid hydrazide* (**11**). **11** (6 g, 0·03 mole) was dissolved in 1 N HCl (36 ml) and $NaNO_2$ soln (2·0 g, 0·041 mole in 50 ml water) added in portions, keeping the temp between 3 and 5°. White crystals which separated were taken up in ether, washed with $NaHCO_3$ aq, with water, dried ($MgSO_4$) and the ether evaporated. The residue (5·1 g, 92·8%) recrystallized from pet ether (b.p. 80–100°) as white, well-developed plates (4·2 g, 76·5%), m.p. 139–139·5°. (Found: C, 65·74; H, 9·45; N, 7·52. $C_{10}H_{17}O_2N$ requires: C, 65·54; H, 9·35; N, 7·65%).

Cis-2-*amino*-cis-4-*t-butylcyclopentanol* (**1**). **12** (4 g, 0·0217 mole) was refluxed with KOH (4 g, 0·07 mole) in 50% EtOH (80 ml) for 3 hr, the mixture evaporated to dryness under reduced pressure and the residue treated with ether. The solution was dried ($MgSO_4$) and evaporated to yield **1** (3·35 g, 97·6%); recrystallized from light petroleum (45–60°), white plates (3·24 g, 94·4%), m.p. 106–106·5°. (Found: C, 68·51; H, 12·28; N, 9·04. $C_9H_{19}ON$ requires: C, 68·74; H, 12·18; N, 8·71%).

Trans-2-*hydroxy*-trans-4-*t-butylcyclopentanecarboxylic* acid (**15**). A mixture of esters **7** + **8** (3·6 g) obtained by catalytic reduction of **6**, freed from the "1,2-*trans*" isomers **9** + **10** by fractional distillation, was refluxed with 40% KOH aq (100 ml) for 10 hr, acidified with HCl, extracted with ether, dried and evaporated. The residue, on repeated crystallizations from light petroleum (45–60°) and then from light petroleum (45–60°)–benzene, afforded **15** (0·74 g, 20·6%) as fine needles, m.p. 90–91°. (Found: C, 64·64; H, 9·80. $C_{10}H_{18}O_3$ requires: C, 64·49; H, 9·74%). The other *trans* isomer, *trans*-2-hydroxy-*cis*-4-t-butylcyclopentanecarboxylic acid (**16**), separated in about 75% purity with 25% **15** and crystallized under identical conditions as thick plates, m.p. 101–102°.

The course of the equilibration **13** ⇌ **15**. **13** (Its methyl ester being homogeneous on a capillary column) was treated as above; samples were withdrawn, transformed into the methyl ester and analyzed. After 2·5 hr the ratio **13**:**15** was 3:7; after 5 hr 2:8, and showed no further change after 12 hr.

Isomerization of trans-2-*hydroxy*-trans-4-*t-butylcyclopentanecarboxylic acid* (**15**). **15** (300 mg) was refluxed in 40% KOH aq (25 ml). After 4 hr the ratio **15**:**13** was 2:8. No dehydration was observed.

Trans-2-*hydroxy*-trans-4-*t-butylcyclopentanecarboxylic acid hydrazide* (**18**). **15** (620 mg) was transformed into the methyl ester with CH_2N_2, then treated with hydrazine hydrate to prepare the hydrazide. The product was crystallized from EtOAc (10 ml) to yield **18** (560 mg, 84·0%), m.p. 134–134·5°. (Found: C, 60·20; H, 10·06. $C_{10}H_{20}O_2N$ requires: C, 59·97; H, 10·06%).

Separation of trans-2-*hydroxy*-trans-4-*t-butylcyclopentanecarboxylic acid hydrazide* (**18**) and trans-2-*hydroxy*-cis-4-*t-butylcyclopentanecarboxylic acid hydrazide* (**19**). A mixture of **9** + **10** (1·6 g) was transformed into hydrazide. The product, taken up in EtOAc (50 ml), was kept at room temp for 2 days. **18**

and **19** separated in two distinctly different crystal forms, and could be manually separated. Fraction (i): well developed light-brown cuboids, m.p. 133–135°; fraction (ii): white plates, m.p. 135–142°. Fraction (i) was recrystallized from EtOAc to give **18**, m.p. 134–135°; it showed no m.p. depression with the hydrazide obtained from **15**. Repeated recrystallization of (ii) from EtOAc yielded **19**, m.p. 155·5–156·5°, markedly less soluble in EtOAc than **18**. (Found: C, 59·78; H, 10·01. $C_{10}H_{22}O_2N$ requires: C, 59·97; H, 10·06%).

Cis- *and* trans-3-*t*-*butylcyclopentanol* (**25**, **26**) *from* 3-*t*-*butylcyclopentanone* (**24**). **24** (21·6 g, 0·154 mole) in EtOH (50 ml) was added dropwise to $NaBH_4$ (4 g, 0·106 mole) in EtOH (300 ml) at 0° in 1 hr. The mixture, kept at 0° for 4 hr and at room temp overnight, was neutralized with AcOH. After EtOH evaporation, the mixture was taken up in ether, washed with 5% $NaHCO_3$ aq, then water, dried ($MgSO_4$) and solvent evaporated giving **25** + **26** (15·5 g, 70·7%). The isomers could not be completely separated by GLC.

3-*t*-*Butylcyclopent*-1-*ene* (**29**) and 4-*t*-*butylcyclopent*-1-*ene* (**30**) *from* cis- *and* trans-3-*t*-*butylcyclopentanol tosylate* (**27**, **28**). The above mixture of **25** and **26** (4·2 g, 0·03 mole) was treated with *p*-TsCl (7·6 g, 0·04 mole) in abs pyridine (25 ml) at 5°. Work-up afforded an oily product (8·3 g, 94·8%), which did not crystallize. The crude tosylate (950 mg) was heated with quinoline (2 ml) in a Hickman flask to 170° bath temp. The product (350 mg, 83·1%) consisted of a 3:2 mixture of **29** and **30**.

4-*t*-*Butylcyclopent*-1,2-*ene*-1-*carboxylic acid* (**22**). A 3:1 mixture of **7** and **8** (52·7 g) was shaken with 10% KOH aq (200 ml) for 1 hr. After removing the impurities with ether, the mixture was acidified (HCl) and ether extracted, the extract dried ($MgSO_4$), evaporated, and the residue crystallized from benzene (200 ml) giving **13** + **14** (42·04 g, 92·6%). The product (35·4 g) was heated to 325° bath temp in a Claisen flask. Water evolved at 200–210°, and **22** distilled with a small quantity of **23** from 285°. The product was taken up in ether and dried ($MgSO_4$). After evaporation the residue (29·45 g, 92·2%) was crystallized from light petroleum (80–100°, 100 ml) to yield **22** (21·85 g), m.p. 104–105°. (Found: C, 71·54; H, 9·39. $C_{10}H_{16}O_2$ requires: C, 71·39; H, 9·59%).

4-*t*-*Butylcyclopent*-1-*ene* (**29**). A mixture of **22** (8·5 g), copper oxide (6·0 g) and quinoline (35 ml) was kept at 225° bath temp in a Claisen flask for 1 hr. The temp was then raised to 245° for a short time, the distillate taken up in light petroleum (45–60°, 150 ml) washed with 3% HCl and water. After drying, solvent was evaporated and the residue distilled. After a fore-run (1·07 g) up to 130° bath temp, the main fraction (4·95 g, 79·7%) $n_D^{20} = 1·4399$ was collected. According to gas chromatography ($AgNO_3$, 50°), the ratio **29**:**30** was 99:1.

Dehydration of trans-2-*hydroxy*-trans-4-*t*-*butylcyclopentanecarboxylic acid* (**15**). **15** (80 mg) was distilled using a Hickman collar flask, and the mixture **22** + **23** obtained was decarboxylated as above, without purification. The product consisted of 96% **29** and 4% **30**.

Trans-4-*t*-*butylcyclopentene*-1,2-*oxide* (**32**) *from* 4-*t*-*butylcyclopent*-1-*ene* (**29**). **29** (2·3 g, 0·024 mole) was kept with perphthalic acid (10·66 g, 0·0585 mole) in ether (100 ml) at 4° for 2 days. The mixture was washed with 5% NaOH aq and with water, dried ($MgSO_4$) and the ether evaporated. The residue was distilled to yield a colourless liquid (2·8 g, 75·3%), $n_D^{20} = 1·4482$, containing 92·1% **32** and 7·9% **31**. (Found: C, 77·17; H, 11·33. $C_9H_{16}O$ requires: C, 77·09; H, 11·50%). Stereohomogeneous **32** was prepared from **37**.

Trans-2-*dimethylamino*-trans-4-*t*-*butylcyclopentanol methiodide* (**37**). *Trans*-2-dimethylamino-*trans*-4-t-butylcyclopentanol (**36**) (1·33 g, 0·006 mole) was refluxed with MeI (3·0 g; 0·021 mole) in MeOH (25 ml) for 1 hr. The mixture was evaporated and crystallized from MeOH–ether as white crystals (1·83 g, 91·1%), m.p. 204–205°. (Found: C, 43·92; H, 8·01. $C_{12}H_{26}NOI$ requires: C, 43·93; H, 8·01%).

Trans-4-*t*-*butylcyclopentene*-1,2-*oxide* (**32**) *from trans*-2-*dimethylamino*-4-trans-*t*-*butylcyclopentanol methiodide* (**37**). From **37** (1·35 g) the base was liberated on an ion-exchange resin and heated in a Hickman flask provided with a cooling jacket, to 150° bath temp in 45 min. Redistillation of product furnished **32** (420 mg, 73·4%). (Found: C, 77·06; H, 11·35. $C_9H_{16}O$ requires: C, 77·09; H, 11·50%).

Trans-2-*amino*-trans-4-*t*-*butylcyclopentanol* (**4**) *from* trans-4-*t*-*butylcyclopentene*-1,2-*oxide* (**32**). A mixture (about 12:1) of *trans*- (**32**) and *cis*-4-t-butylcyclopentene-1,2-oxide (**31**) (2·45 g) was heated with 0·88 NH_4OH (55 ml) at 160° for 5 hr, extracted with ether, the extract dried (KOH), and evaporated to yield white crystals (2·42 g, 89·6%), which after three recrystallizations from light petroleum (45–60°) gave translucent prisms (1·87 g, 69·2%), m.p. 68–69°. (Found: C, 68·62; H, 12·40; 8·87. $C_9H_{19}ON$ requires: C, 68·74; H, 12·18; N, 8·71%).

Trans-2-*dimethylamino*-trans-4-*t*-*butylcyclopentanol* (**36**). **1** (2·1 g) was refluxed with 36% formaldehyde aq (70 ml) for 24 hr. Work-up afforded **36** (2·1 g, 84·9%), recrystallized from light petroleum (45–60°), m.p. 61·5–62·5°. (Found: C, 71·28; H, 12·49; N, 7·38. $C_{11}H_{23}NO$ requires: C, 71·29; H, 12·51; N, 7·56%).

The hydrochloride of **36**: white crystals from abs EtOH-ether, m.p. 268–268·5°. (Found: C, 59·70; H, 10·91; Cl^-, 15·89, $C_{11}H_{24}NOCl$ requires: C, 59·57; H, 10·91; Cl^-, 10·99%).

Trans-2-*benzamido*-trans-4-*t-butylcyclopentanol* (**20**). Schotten-Baumann benzoylation of **4** (1·6 g) yielded **20** (2·15 g, 80·8%), m.p. 115–116° as plates from benzene–light petroleum (80–100°). (Found: C, 73·35; H, 8·61, N, 5·54. $C_{16}H_{23}O_2N$ requires: C, 73·53; H, 8·87; N, 5·36%).

2-*Phenyl*-cis-4,5-(cis-2′-*t-butyl-trimethylene*)-Δ^2-*oxazoline* (**21**). **20** (720 mg) was added to cooled (0°) $SOCl_2$ (4 ml) in portions under shaking. The mixture was kept at room temp for 1 hr, $SOCl_2$ removed at 30 mm, the residue taken up in water, made alkaline (Na_2CO_3) and ether extracted. The extract was dried ($MgSO_4$), evaporated and the residue distilled at 0·4 mm to give **21** (260 mg, 53·7%), m.p. 84–85·5° (ether). (Found: C, 78·60; H, 8·54; N, 6·03. $C_{16}H_{21}ON$ requires: C, 78·94; H, 8·70; N, 5·70%). The picrate of **21** crystallized from EtOH, m.p. 170–170·5°. (Found: C, 55·86; H, 5·36; N, 11·73. $C_{22}H_{24}O_8N_4$ requires: C, 55·93; H, 5·12; N, 11·86%).

Preparation of cis-2-*amino*-cis-4-*t-butylcyclopentanol* (**1**) *from the oxazoline* **21**. **21** (210 mg) was refluxed with EtOH (10 ml) and conc. HCl (10 ml) for 10 hr. The mixture was evaporated at 30 mm, ether extracted, made alkaline (KOH) and the product ether extracted. The extract was dried (KOH) and evaporated to yield **1** (130 mg, 95·8%), m.p. 106–106·5° (from light petroleum, 45–60°). A change of the crystal form was observed under the microscope at 85–92°. No m.p. depression was shown with **1** prepared from **11**.

Trans-2-*bromo*-cis-4-*t-butylcyclopentanol acetate* (**33**). Freshly prepared, dry, powdered AgOAc (30·5 g, 0·183 mole) was suspended in CCl_4 (50 ml), cooled to −15° and Br_2 (19·5 g, 0·082 mole) in CCl_4 (50 ml) added in portions with stirring. The mixture was shaken for 5 min and this acetylhypobromite soln was immediately filtered into a cooled soln of **29** (11·0 g, 0·0885 mole) in light petroleum (45–60°, 50 ml). The mixture warmed up, indicating reaction. Evaporation of solvent at 30 mm afforded light yellow liquid (20·05 g, 95·0%) containing, besides **33**, some 1,2-dibromo-4-t-butylcyclopentane. This crude product was used for further reactions. A sample was distilled for analysis, b.p. 135–136°/15 mm, $n_D^{20} = 1·4779$. (Found: C, 49·52; H, 7·14; Br, 31·57. $C_{11}H_{19}O_2Br$ requires: C, 50·20; H, 7·26; Br, 30·37%).

Cis-4-*t-butylcyclopentene*-1,2-*oxide* (**31**). **33** (21·3 g) was heated with 50% KOH aq (150 ml) in a Claisen flask; the epoxide formed distilled with the steam. When no more oily drops could be observed (1 hr), the distillate was ether extracted, the extract dried ($MgSO_4$) and the solvent evaporated. The residue was distilled to give homogeneous **31** (7·46 g, 65·7%), b.p. 75–76°/15 mm, $n_D^{20} = 1·4497$; no traces of **32** could be detected by gas chromatography. (Found: C, 76·73; H, 11·30. $C_9H_{16}O$ requires: C, 77·09; H, 11·50%).

Trans-2-*amino*-cis-4-*t-butylcyclopentanol* (**3**). **31** (3·92 g) was heated with 0·88 NH_4OH aq at 170° for 6 hr. Work-up, as described above for preparation of **1**, afforded **3** (4·15 g, 94·4%), m.p. 64–65°. A sample was recrystallized twice from light petroleum (45–60°); the m.p. rose to 65·5–66·0°. **3** absorbs CO_2 from the air very rapidly, therefore the analytical data correspond only approximately to the calcd values, even when analyzing a sample immediately after distillation (b.p. 130–132°/10 mm). (Found: C, 68·15; H, 12·13; N, 8·25. $C_9H_{19}ON$ requires: C, 68·74; H, 12·18; N·91%). The analysis of the N-benzoyl derivative (**34**) was satisfactory.

Trans-2-*benzamido*-cis-4-*t-butylcyclopentanol* (**34**). **3** (4·15 g) was benzoylated (Schotten-Baumann) to give **34** (5·92 g, 85·8%), m.p. 126–127°. An analytical sample, m.p. 127·5–128°, was recrystallized twice from benzene-light petroleum (60–80°). (Found: C, 73·62; H, 8·86; N, 5·37. $C_{16}H_{23}O_2N$ requires: C, 73·53; H, 8·87; N, 5·36%).

2-*Phenyl*-cis-4,5-(trans-2′-*t-butyl-trimethylene*)-Δ^2-*oxazoline* (**35**). **34** (3·55 g) was treated with $SOCl_2$ (20 ml) as described above for reaction **20** → **21**. Work-up afforded **35** (3·1 g, 93·8%), m.p. 67–69°. An analytical sample, m.p. 68–69°, was recrystallized twice from light petroleum (60–80°). (Found: C, 78·73; H, 8·85; N, 5·61. $C_{16}H_{21}ON$ requires: C, 78·97; H, 8·70; N, 5·76%).

Cis-2-*amino*-trans-4-*t-butylcyclopentanol* (**2**). **35** (2·6 g) was refluxed with conc. HCl (35 ml) and EtOH (35 ml) for 10 hr. Work-up gave **2** (1·15 g, 92·3%), m.p. 84·5–85·5°. Recrystallization of a sample from light petroleum (45–60°) raised the m.p. to 88·5–89°. (Found: C, 68·98; H, 12·39: N, 8·79. $C_9H_{19}ON$ requires: C, 68·74; H, 12·18; N, 8·91%).

Acknowledgement—An important part of these results was obtained by the author (B.G.) during his stay in Prague. A grant of the Hungarian Ministry of Education is gratefully acknowledged. The authors are indebted to the late Professor J. Sicher for his kind interest and helpful discussions. Thanks are due to Mr. L. Baštař for the gas chromatographical analyses, to Dr. M. Ryba for performing the fractional distillations, to

Dr. A. Vítek and Dr. S. Vašičková for measuring the IR spectra, to the Analytical Department of the Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science (Head of the Department Dr. J. Horáček) for the microanalyses, and to P. Marešovská for technical assistance.

REFERENCES

[1] Part XII (V): G. Bernáth, K. L. Láng, Gy. Göndös, P. Márai and K. Kovács, *Acta Chim. (Budapest)* in press; G. Bernáth, K. L. Láng, Gy. Göndös, P. Márai and K. Kovács, *Tetrahedron Letters* 4441 (1968)
[2] D. J. Pasto and D. R. Rao, *J. Am. Chem. Soc.* **92**, 5151 (1970)
[3] J. Sicher, F. Šipoš and M. Tichý, *Coll. Czech. Chem. Comm.* **26**, 847 (1961)
[4] J. Sicher, M. Tichý, F. Šipoš and M. Pánková, *Ibid.* **26**, 2416 (1961)
[5] I. Lillien and K. Khaleeluddin, *Chem. & Ind.* 1028 (1964)
[6] J. C. Richer and C. Girlardeau, *Can. J. Chem.* **43**, 3418 (1965)
[7] G. M. Kauffman, *Diss. Abstr.* **27**, 1417–B (1966)
[8] G. Bernáth, P. Sohár, K. L. Láng, I. Tornyai and Ö. K. J. Kovács, *Acta Chim. (Budapest)* **64**, 81 (1970)
[9] G. Bernáth, Gy. Göndös, P. Márai and L. Gera, *Ibid.* in press
[10] G. Bernáth, K. Kovács and K. L. Láng, *Ibid.* **64**, 183 (1970)
[11] H. Narsaki and N. Ito, *Repts. Govt. Chem. Ind. Research Inst. Tokyo* **46**, 199 (1951): *Chem. Abstr.* **46**, 454b (1952)
[12] N. S. Grossley, A. C. Darby, H. B. Henbest, J. J. McCullough, B. Nicholls and M. F. Stewart, *Tetrahedron Letters* 398 (1961)
[13] H. B. Henbest, *Proc. Chem. Soc.* 159 (1963)
[14] W. S. Johnson and E. N. Schubert, *J. Am. Chem. Soc.* **72**, 2187 (1960)
[15] H. B. Henbest and J. J. McCullough, *Proc. Chem.* Soc. 74 (1962)
[16] C. H. Robinson, *J. Am. Chem. Soc.* **81**, 2195 (1959)