STEREOCHEMISTRY OF CYCLIC COMPOUNDS

COMMUNICATION 56. STERIC ORIENTATION IN THE DIENE CONDENSATION OF 1-(1-CHLOROVINYL)CYCLOHEXENE WITH trans-1-NITROPROPENE

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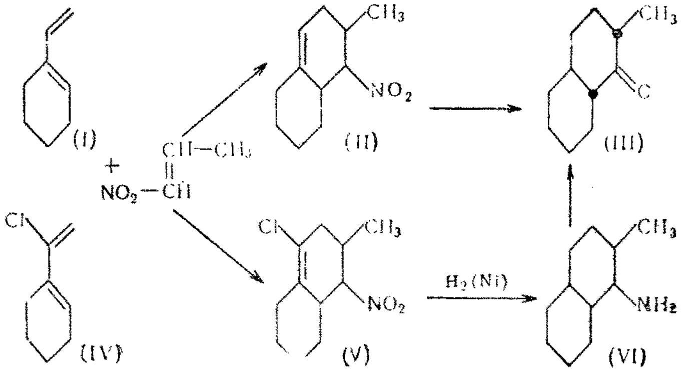
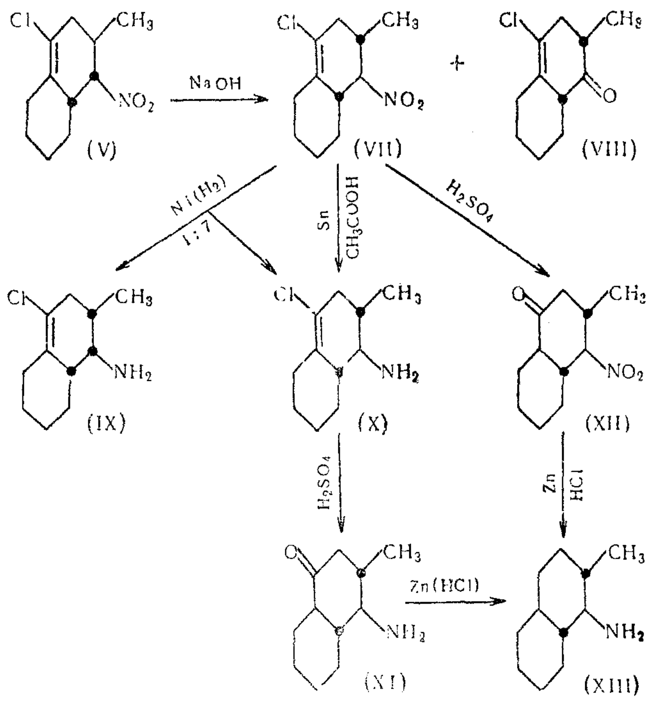
As shown in the preceding communication [1], the diene condensation of 1-vinylcyclohexene (I) with trans-1-nitropropene leads to the liquid adduct (II), whose structure was proved by its conversion into the trans-2-methyldecalone (III) [2]. However, the configuration of the adduct formed and therefore the steric orientation in the condensation remained unproved because it was not altogether sure that the reaction product was homogeneous.

With the object of elucidating the question of the stereochemistry of diene synthesis with the participation of trans nitro dienophiles we have studied the condensation of trans-1-nitropropene with 1-(1-chlorovinyl)cyclohexene (IV), and the results obtained are examined in this paper. It was shown that, when a mixture of these components is heated in benzene, a homogeneous crystalline adduct of m.p. 58° (V) is formed in about 60% yield, and the chemical transformations of this enabled us to prove not only its structure, but also its configuration.



It was found that exhaustive hydrogenation of this adduct over a nickel catalyst proceeds with simultaneous hydrogenolysis, and after the absorption of five molecular proportions of hydrogen a mixture of stereoisomeric amines (VI) is formed and can be isolated as their hydrochlorides. By the reaction of this mixture with N-chlorosuccinimide by the previously described method [3] the known trans-2-methyldecalone (III) was obtained in good yield, which proves the structure of the adduct (V) unequivocally. We succeeded in determining the configuration of the adduct (V) by studying the chemical transformations of the compounds formed in its alkaline isomerization. It was found that, when boiled for a short time (three hours) with aqueous sodium hydroxide, the adduct (V) gives the isomeric crystalline substance (VII), m.p. 65°, which is obtained also under more severe alkaline-hydrolysis conditions (boiling for eight hours). In this last case the isomer (VII) was accompanied by a small amount (10-15%) of the normal product of the Nef reaction (VIII), which was characterized as its 2,4-dinitrophenylhydrazone. Attempts to carry out the Nef reaction under still more severe conditions were not successful: only polymerization products were obtained.

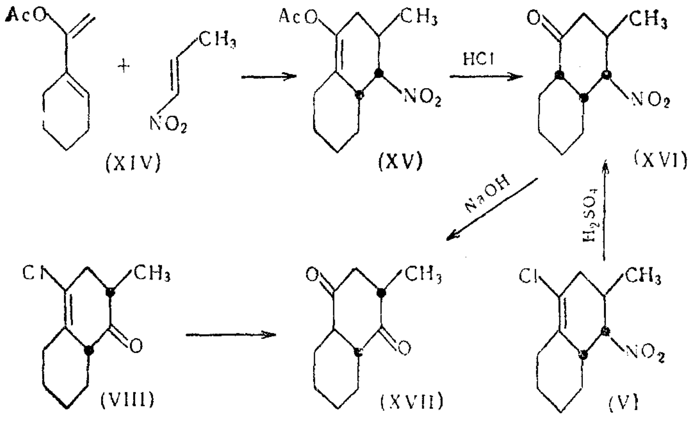
It is extremely improbable that the conversion of the adduct (V) into its isomer (VII) under alkaline conditions proceeds as a result of the isomerization of the trans substituents into the less favored cis arrangement. It was therefore more likely that these isomers have syn-trans and anti-trans configurations. As the latter is thermodynamically



more favored it is quite probable that it corresponds to the isomer (VII). To resolve this question we studied some chemical transformations of this isomerization product, and these provided confirmation of the view advanced above.

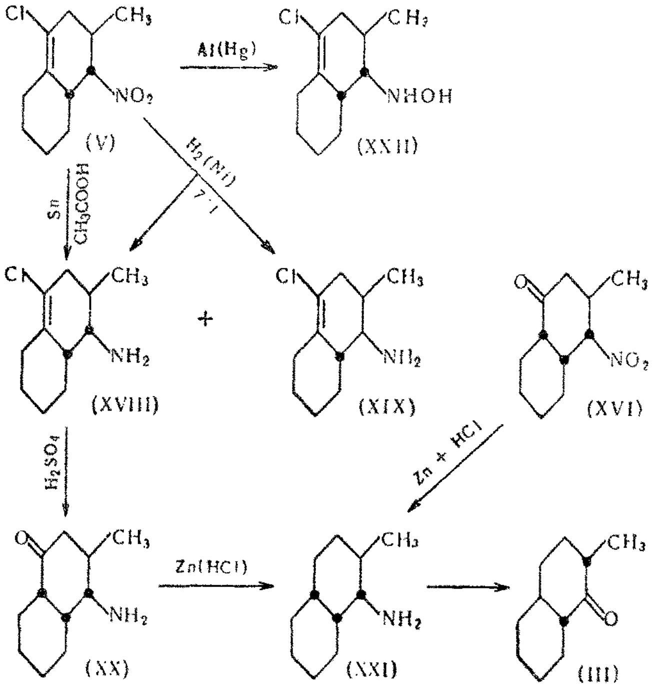
It was shown that, when the catalytic hydrogenation of the isomer (VII) over a nickel catalyst was interrupted after the absorption of three molecular proportions of hydrogen, a mixture (about 1 : 7) of the isomeric chloro amines (IX) and (X) was formed. The second of these was obtained as the sole reaction product also in the reduction of (VII) with tin and acetic acid. Since such reduction proceeds with preservation of the configuration of the original nitro group, as has been shown rigorously previously [4], the chloro amine (X) formed under these conditions must have the same spatial structure as the nitro chloro compound (VII). On this basis we carried out the acid hydrolysis of the chlorovinyl groups in both these compounds, which, as is well known, proceeds with formation of the more stable trans-fusion of the rings and should not touch the configurations of other centers. Clemmensen reduction of the ketones formed (XI) and (XII) gave trans-anti-trans-2-methyl-1-decalylamine (XIII), which was found to be identical with previously described preparations in its crystalline derivatives [1]. The whole of this sequence of stereospecific transformations enables us to consider that the isomer (VII) does indeed have the anti-trans configuration and that the adduct (V) has therefore the syn-trans configuration.

This result shows that the condensation of 1-(1-chlorovinyl)cyclohexene (I) with trans-1-nitropropene proceeds in accordance with the general structural and steric laws of the diene synthesis, as we have noted previously for the case of other dienophiles [5]. The same steric orientation is found also in the condensation of 1-(1-acetoxyvinyl)-cyclohexene (XIV) with trans-1-nitropropene, for the liquid adduct formed (XV) gave on acid hydrolysis the same nitro ketone (XVI) as was formed in the hydrolysis of the nitro chloro adduct (V).



Under the conditions of the Nef reaction the nitro ketone (XVI) is readily converted into the corresponding diketone (XVII), which is obtained also from the above-described chloro ketone (VIII). Since in both these cases two different centers of asymmetry are affected, it is quite natural to expect that one and the same diketone (XVII) will be formed; (XVII) must have the thermodynamically more favored configuration with trans-fusion of the rings and an equatorial position of the methyl group. As regards the spatial structure of the nitro ketone (XVI) itself, we have assumed this on the basis of general conformational laws, according to which in polycyclic systems the cis-syn-trans configuration is more stable than the trans-syn-trans configuration [6]. On this basis it is more likely that the nitro ketone (XVI) has the cis-syn-trans configuration and that its formation in the acid hydrolysis of the adducts (V) and (XV) proceeds without isomerization at the ring-fusion positions, though this inference cannot yet be considered as proved.

For the original adduct (V) we studied some chemical transformations having definite interest from the point of view of synthesis.



As in the case of the isomer (VII) the catalytic hydrogenation of the adduct (V) over a nickel catalyst went nonselectively and led to a mixture of the chloro amines (XVIII) and (XIX) in relative amounts of about 7 : 1. One of these isomers (XVIII) was obtained also in the stereospecific reduction of the adduct (V) with tin and acetic acid and so had the same syn-trans configuration. The formation of the isomeric chloro amines (XVIII) and (XIX), different from the above-described chloro amines (IX) and (X), provides further confirmation of the configuration of the isomeric adduct (VII). Acid hydrolysis of the chloro amine (XVIII) readily gave the corresponding amino ketone (XX), by the Clemmensen reduction of which 2-methyl-1-decalylamine (XXI) was formed. Both these compounds were taken to have the cis-syn-trans configuration on the basis of the same assumptions as those considered above in the case of the nitro ketone (XVI). We succeeded in confirming that they belonged to the same steric series by the Clemmensen reduction of the nitro ketone (XVI) to the decalylamine (XXI).

The reduction of the adduct (V) with aluminum amalgam is of undoubted preparative interest: it leads in good yield to the compound (XXII), which according to the elementary analysis of its hydrochloride is a hydroxylamine derivative.

EXPERIMENTAL

Condensation of 1-(1-Chlorovinyl)cyclohexene (IV) with trans-1-Nitropropene. A mixture of 42 g of 1-(1-chlorovinyl)cyclohexene (IV) [5] and 40.3 g of trans-1-nitropropene [7] was boiled for eight hours in 100 ml of dry benzene in presence of hydroquinone. Solvent and unchanged reactants were distilled off, and vacuum distillation of the residue gave 42.3 g of reaction product of b.p. 155-160° (10 mm), which rapidly crystallized out. The crystals were washed on the filter with cold methanol and dried. We obtained 38.3 g of syn-trans-1-nitro-2-methyl-4-chloro-Δ^4-octalin (V), which melted constantly at 57-58° (from methanol). Found: C 57.54, 57.46; H 7.19. 7.20; Cl 15.49, 15.44%. $C_{11}H_{17}ClNO_2$. Calculated: C 57.26; H 7.42; Cl 15.36%. The infrared spectrum of the adduct (V) contained frequencies characteristic for the NO_2 group at 1556 and 1380 cm^{-1} (in CCl_4).

Proof of the Structure of the Adduct (V). 2 g of the adduct (V) was hydrogenated in 25 ml of methanol over Raney nickel that had been first saturated with hydrogen. After the absorption of five molecular proportions of hydrogen the catalyst was filtered off and the filtrate was vacuum-evaporated to dryness. The resulting crystalline mixture (1.8 g) of hydrochlorides of stereoisomer of the amine (VI), m.p. 182-188°, could not be separated by fractional crystallization. By treatment with aqueous sodium hydroxide solution 1 g of the mixture was converted into a mixture of amines (VI) (0.8 g), which was dissolved in 45 ml of methylene chloride. To the solution we added 0.64 g of N-chlorosuccinimide (until the reaction was neutral). After one hour the solution was washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness. The resulting semicrystalline mixture of chloro amines was boiled for 90 minutes with sodium methoxide solution (from 0.4 g of sodium) in 20 ml of absolute methanol. Solvent was removed, and the residue was acidified with 2 N H_2SO_4. The oil that separated was extracted with ether and boiled with dilute (1 : 1) hydrochloric acid; we obtained 0.5 g of the trans-2-methyldecalone (III), whose 2,4-dinitrophenylhydrazone had m.p. 218-220°, undepressed by admixture of a known sample [1].

Alkaline Isomerization of the Adduct (V). a) 10 g of the adduct (V) was boiled for three hours with a solution of 3.5 g of sodium hydroxide in 50 ml of water. The cooled solution was extracted with ether and acidified to Congo Red with 2 N H_2SO_4. Extraction with ether gave an oil which crystallized out on standing. The crystals were washed on the filter with petroleum ether, and we obtained 8.2 g of anti-trans-1-nitro-2-methyl-4-chloro-Δ^4-octalin (VII), m.p. 65-65.5° (from methanol). Found: C 57.58, 57.55; H 7.10, 7.07%. $C_{11}H_{17}ClNO_2$. Calculated: C 57.26; H 7.42%. ν_{max} (NO_2) 1550 and 1367 cm^{-1} (in CCl_4).

b) 5 g of the adduct (V) was boiled with 1.75 g of sodium hydroxide in 25 ml of water for eight hours. After analogous treatment we obtained 3.5 g of the nitrooctalin (VII) together with 0.65 g of an oily reaction product which gave 0.45 g of the 2,4-dinitrophenylhydrazone of 2-methyl-4-chloro-Δ^4-octal-1-one (VIII), m. p. 122-123° (from a 1 : 1 mixture of chloroform and methanol). Found: C 53.72, 53.74; H 5.06, 4.98%. $C_{17}H_{19}ClN_4O_4$. Calculated: C 53.91; H 5.05%.

Preparation of the Isomeric Chloro Amines (IX) and (X). a) 4.4 g of the isomeric adduct (VII) was hydrogenated over Raney nickel in 30 ml of ethyl acetate. After the absorption of three molecular proportion of hydrogen, hydrogenation was stopped and the catalyst was filtered off. After evaporation we obtained an oil, which partially crystallized out. The crystals were filtered off and washed with ether. We isolated 0.4 g of the hydrochloride of syn-cis-1-amino-2-methyl-4-chloro-Δ^4-octalin (IX), m.p. 266-267° (decomp.) (from a 1 : 3 mixture of methanol and ether). Found: C 55.98, 56.03; H 8.11, 8.08%. $C_{11}H_{19}NCl_2$. Calculated: C 55.93; H 8.07%.

After the evaporation of the mother liquor we obtained 3.4 g of liquid anti-trans-1-amino-2-methyl-4-chloro-Δ^4-octalin (X), which gave a hydrochloride of m.p. 253-254° (from a mixture of methanol and ether). The chloro amine (X) was converted also into the N-acetyl derivative, m.p. 176-177° (from a mixture of diethyl ether and petroleum ether), and the N-benzoyl derivative, m.p. 199-200° (from methanol). Found: C 70.81, 71.00; H 7.36, 7.38%. $C_{18}H_{22}NOCl_2$. Calculated: C 71.15; H 7.29%.

b) 3 g of the isomer (VII) was boiled with stirring with 1.8 g of finely cut tin in 15 ml of glacial acetic acid for three hours. The solution was cooled and poured into excess of 40% aqueous potassium hydroxide solution. By ether extraction we obtained 2.2 g of the chloro amine (X), the crystalline derivatives of which were identical with those described above.

Acid hydrolysis of the Isomeric Adduct (VII) and the Chloro Amine (X). a) 3 g of the isomer (VII) was treated with 9 ml of concentrated sulfuric acid at 0-5° for four hours. The solution was poured into water, and the mixture was kept for 30 minutes at 50°. Extraction with ether gave 1.6 g of the oily nitro decalone (XII), which gave a 2,4-dinitrophenylhydrazone of m.p. 238-239° (from a 1 : 1 mixture of methanol and chloroform) and a semicarbazone of m.p. 216-217° (from methanol). Found: N 20.99; 21.03%. $C_{12}H_{20}N_4O_3$. Calculated: N 20.89%.

b) Under analogous conditions 1 g of the chloro amine (X) was converted into 0.55 g of the liquid aminodecalone (XI); the sulfate of the 2,4-dinitrophenylhydrazone had m.p. 184-185° (from methanol). Found: C 44.21; H 5.32%. $C_{17}H_{25}N_5O_8S$. Calculated: C 44.43; H 5.48%.

trans-anti-trans-2-Methyl-1-decalylamine (XIII). a) 1.3 g of the above-described nitrodecalone (XII) was boiled for 25 hours with 4.9 g of amalgamated zinc and 28 ml of dilute (1 : 1) hydrochloric acid. The solution was filtered and vacuum-evaporated. After alkaline treatment we isolated 0.6 g of the liquid decalylamine (XIII), which gave a hydrochloride of m.p. 239-240° and an N-acetyl derivative of m.p. 153-155°. Both derivatives were found to be identical with samples synthesized earlier [1].

b) By reduction in an analogous manner, from 1 g of the aminodecalone (XI) we obtained 0.65 g of the decalylamine (XIII), which gave derivatives identical with the above-described samples.

Condensation of 1-(1-Acetoxyvinyl)cyclohexene (XIV) with trans-1-Nitropropene. A solution of 5 g of 1-(1-acetoxyvinyl)cyclohexene (XIV) [8] and 7 g of trans-1-nitropropene in 25 ml of benzene was boiled for 25 hours in presence of pyrogallol. Solvent and unchanged reactants were distilled off, and distillation of the residue gave 4.95 g (62%) of liquid syn-trans-1-nitro-2-methyl-4-acetoxy-Δ^4-octalin (XV); b.p. 153-154° (2 mm); n_D^{18} 1.4975. Found: C 61.35, 61.43; H 7.31, 7.42%. $C_{13}H_{19}NO_4$. Calculated: C 61.64; H 7.56%.

Acid Hydrolysis of the Adducts (V) and (XV). a) A mixture of 2 g of the adduct (V) and 14 ml of concentrated sulfuric acid was left at 0° for five hours. After the above-described treatment we obtained 1.1 g of oily nitrodecalone (XVI), b.p. 155-157° (3 mm), which gave a 2,4-dinitrophenylhydrazone of m.p. 164.5-166° (from a 2 : 1 mixture of chloroform and methanol) and a semicarbazone of m.p. 199-200° (from methanol). Found: N 21.06, 21.00%. $C_{12}H_{20}N_4O_3$. Calculated: N 20.89%.

b) 2 g of the adduct (XV) was boiled in 20 ml of methanol containing 2 ml of hydrochloric acid for 15 minutes, and the mixture was then poured into water. Extraction with ether gave 1.9 g of the liquid nitrodecalone (XVI), whose semicarbazone had m.p. 198-199°, undepressed by admixture of the sample obtained above.

trans-2-Methyl-1,4-decalindione (XVIII). a) 1 g of the nitrodecalin (XVI) was boiled for three hours with 0.3 g of sodium hydroxide in 10 ml of water, and the resulting solution was added to excess of 2 N sulfuric acid. After one hour the mixture was extracted with ether, and we obtained 0.6 g of an oil, which gave a bis(2,4-dinitrophenylhydrazone) of m.p. 212-213° (from a 1 : 1 mixture of chloroform and methanol). Found: C 51.51; H 4.30%. $C_{23}H_{22}N_8O_8$. Calculated: C 51.29; H 4.12%.

b) A mixture of 0.5 g of the chlorooctalone (VIII) and 3 ml of concentrated sulfuric acid was left at 0-5° for 90 minutes. After treatment we isolated 0.25 g of an oil, which gave 0.2 g of a bis(2,4-dinitrophenylhydrazone) of m.p. 209-210.5°, identical with the sample prepared above.

Reduction of the Adduct (V). a) 10 g of the adduct (V) was hydrogenated over Raney nickel in 100 ml of ethyl acetate until three molecular proportions of hydrogen had been absorbed. Catalyst was filtered off, and the filtrate was evaporated to dryness. The partially crystallized oily residue was filtered, and the crystals were washed with ether on the filter. We obtained 1 g of the hydrochloride of anti-cis-2-methyl-4-chloro-Δ^4-octalyl-1-amine (XIX), m.p. 299-300° (from a 1 : 1 mixture of methanol and ether). Found: C 56.06, 55.99; H 8.21, 8.22%. $C_{11}H_{19}NCl_2$. Calculated: C 55.93; H 8.07%. From this hydrochloride by the usual method we prepared the N-benzoyl derivative, m.p. 157-157.5° (from methanol). Found: C 70.81, 71.01; H 7.43, 7.37%. $C_{18}H_{22}NOCl$. Calculated: C 71.15; H 7.29%.

The mother liquor remaining after the removal of the hydrochloride (XIX) was evaporated to dryness, and we obtained 7.1 g of syn-trans-2-methyl-4-chloro-Δ^4-octalyl-1-amine (XVIII); b.p. 100-102.5° (3 mm); n_D^{18} 1.5276; this gave an N-benzoyl derivative of m.p. 199-200° (from methanol). Found: C 71.28, 71.40; H 7.23, 7.37; Cl 11.43, 11.56%. $C_{18}H_{22}NOCl$. Calculated: C 71.15; H 7.29; Cl 11.67%.

The hydrochloride of the amine (XVIII) had m.p. 248-249° (from a 1 : 2 mixture of methanol and ether). Found: C 56.06, 56.08; H 8.04, 8.22; Cl 29.90, 29.78%. $C_{11}H_{19}NCl_2$. Calculated: C 55.93; H 8.07; Cl 29.99%. The N-acetyl derivative had m.p. 148-149° (from ether on cooling).

b) 1 g of the adduct (V) was boiled with 0.6 g of tin turnings and 7 ml of glacial acetic acid until the tin had dissolved completely (80 minutes). The mixture was poured into excess of an aqueous solution of potassium hydroxide, and extraction with ether gave 0.85 g of the chloro amine (XVIII), which gave derivatives identical with those obtained above.

c) 0.6 g of mercuric chloride was added with stirring to a suspension of 0.6 g of aluminum powder in 20 ml of dry ether, and after 15 minutes a solution of 1.5 g of the adduct (V) in 10 ml of dry ether was added. 2 ml of water was added gradually. The temperature rose to the boil, and boiling was maintained for two hours. The suspended matter was filtered off, and the mother solution was evaporated to dryness. We obtained 1.3 g of oily syn-trams-1-(hydroxyamino)-2-methyl-4-chloro-Δ^4-octalin (XXII), which gave a hydrochloride of m.p. 167-168° (from a 1 : 3 mixture of methanol and ether). Found: C 52.52, 52.48; H 7.59, 7.66%. $C_{11}H_{19}NOCl_2$. Calculated: C 52.38; H 7.59%.

Acid Hydrolysis of the Chloro Amine (XVIII). 1.4 g of the chloro amine (XVIII) was treated with 6 ml of concentrated sulfuric acid at 5-10° for two hours. The mixture was diluted with water and made alkaline, and ether extraction then gave 0.9 g of the liquid aminodecalone (XX). The hydrochloride of the 2,4-dinitrophenylhydrazone had m.p. 252-253° (from a 1 : 1 mixture of chloroform and methanol). Found: N 15.43, 15.64%. $C_{17}H_{24}N_5ClO_4$. Calculated: N 15.58%. The sulfate of the 2,4-dinitrophenylhydrazone of (XVIII) had m.p. 228-229° (from methanol).

Transformations of the Nitro- and Amino-decalones (XVI) and (XX). a) 1 g of the nitrodecalone (XVI) was boiled for 25 hours with 3.5 g of amalgamated zinc in 20 ml of dilute (1 : 1) hydrochloric acid. The solution was filtered, extracted with ether, and vacuum-evaporated to dryness. The residue was treated with aqueous potassium hydroxide solution, and extraction with ether gave 0.75 g of liquid cis-syn-trans-2-methyl-1-decalylamine (XXI), which gave a hydrochloride having decomp. temp. 222-223° (from a 2 : 1 mixture of methanol and ether). The N-benzoyl derivative had m.p. 195.5-197° (from methanol). The N-acetyl derivative had m.p. 242-243° (from methanol or a 1 : 1 mixture of diethyl ether and petroleum ether). Found: C 74.41; H 10.93%. $C_{13}H_{23}NO$. Calculated: C 74.59; H 11.08%.

b) 1 g of the aminodecalone (XX) was subjected to Clemmensen reduction under analogous conditions and we obtained 0.6 g of the decalylamine (XXI), which gave derivatives identical with those obtained above.

From 0.4 g of the decalylamine (XXI) under the conditions described for the amine (VI) we obtained 0.3 g of the 2,4-dinitrophenylhydrazone of (III), m.p. 219-220°, identical to a known sample.

SUMMARY

1. A study was made of structural and spatial orientation in the diene condensation of 1-(1-chlorovinyl)cyclohexene (IV) with trans-1-nitropropene, and the configurations of the adduct (V) and its isomer (VII) were proved.

2. The laws underlying the transformations and stereochemistry of the products formed in the acid hydrolysis and reduction of the isomeric chloronitrooctalins (V) and (VII) were elucidated.

LITERATURE CITED

1. G. M. Segal', L. P. Rybkina, and V. F. Kucherov, Izv. AN SSSR. Otd. khim. n. 1253 (1963).
2. W. J. Bailey and M. Madoff, J. Amer. Chem. Soc. 76, 2707 (1954); J. W. Cook and C. A. Lawrence, J. Chem. Soc. 817 (1937).
3. H. Ruschig, W. Fritsch, J. Schmidt-Thome, and W. Haede, Chem. Ber. 88, 883 (1955).
4. N. Kornblum and L. Fishbein, J. Amer. Chem. Soc. 77, 6266 (1955); J. Weinstock and N. Schwartz, J. Organ. Chem. 26, 5247 (1961).
5. G. M. Segal', L. P. Rybkina, and V. F. Kucherov, Izv. AN SSSR. Otd. khim. n. 1424 (1962).
6. W. Klyne, Progress in Stereochemistry, London, 1, 36 (1954).
7. E. Schmidt and G. Rutz, Ber. 61, 2142 (1928); E. B. Tamelen and R. J. van Thiede, J. Amer. Chem. Soc. 74, 2615 (1952).
8. I. N. Nazarov, V. F. Kucherov, V. M. Andreev and G. M. Segal', Dokl. AN SSSR 104, 729 (1955).
