## STRUCTURAL ORIENTATION IN THE DIENE CONDENSATION OF trans-PIPERYLENE WITH SOME NITRO DIENOPHILES

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A. A. Dudinskaya, S. S. Novikov, and G. A. Shvekhgeimer

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We have previously [1] described the condensation of trans-piperylene with some 1,2-disubstituted nitro dienophiles of type RCH =  $CHNO_2$ 



in which R = H,  $CH_3$ ,  $C_6H_5$ ,  $COOCH_3$ ,  $CCl_3$ .

We here report a study of structural orientation in these reactions. In the general case of the condensation of a diene substituted in the 1-position with an unsymmetrically substituted dienophile a mixture of two structurally isomeric adducts, ortho and meta, may be formed, and each of these, in their turn, may exist in the form of two geometric isomers with cis and trans arrangements of the substituents relative to the plane of the ring



Numerous experimental data show that in most cases under mild conditions 1-substituted dienes form adducts with an ortho-cis or meta-cis arrangement of substituents [2, 3]. The study of structural orientation in the diene synthesis is interesting in all cases of the practical application of this reaction, but also for the elucidation of the mechanism of the diene synthesis. As regards the diene condensation of piperylene with unsaturated nitro compounds, when we started this work only the data of Wildman and co-workers [4] were available, and these showed that in the condensation of piperylene with  $\beta$ -nitrostyrene two isomers, ortho and meta, are formed. Later [5], the condensation of piperylene with  $\beta$ -nitrostyrene two isomers, of the mixture and the structures of the adducts the product of the condensation of trans-piperylene with nitroethylene was subjected to the Nef reaction to convert nitro into keto. The ketone obtained gave one semicarbazone, which was found to be identical to the semicarbazone of 2-methyl-3-cyclohexen-1-one [6]. Also, the 2,4-dinitrophenylhydrazone of a ketone was obtained, and by chromatography on alumina and fractional crystallization we could detect only one isomer. It may be considered, therefore, that in the condensation of nitroethylene with trans-piperylene only 3-methyl-4-nitrocyclohexene (the ortho isomer) is formed \*.

\* The terms "ortho" and "meta" are to be understood as referring to the orientation of the methyl of trans-piperylene relative to the nitro of the dienophile.

All the condensations of 1, 2-disubstituted nitro dienophiles (1-nitropropene,  $\beta$ -nitrostyrene, methyl 3-nitroacrylate, and 3, 3, 3-trichloro-1-nitropropene), whose trans configuration was proved earlier [7], were conducted under comparable conditions by heating the reactants together at 100-110° for 12 h. It was found that in the condensation of trans-piperylene with 1-nitropropene a mixture of structurally isomeric adducts is formed, whose structures were established in the following way: the condensation product was hydrogenated over an Adams platinum catalyst until one molecular proportion of hydrogen had been absorbed and was then converted by the Nef reaction into a mixture of ketones. The mixture of 2,4-dinitrophenylhydrazones prepared from this was separated by fractional crystallization into two isomers: the 2,4-dinitrophenylhydrazone of 2,6-dimethylcyclohexanone and the 2,4-dinitrophenylhydrazone of 2,3-dimethylcyclohexanone, obtained in 14:1 proportions.



The composition of the product of the condensation of trans-piperylene with  $\beta$ -nitrostyrene and the structures of the adducts were established in accordance with the scheme proposed by Wildman and co-workers [3]. In the recrystallization of the mixture of adducts from ethanol we obtained two isomers (ortho and meta in 12:1 proportions), the structures of which were proved earlier.



The compositions of the mixtures obtained in the condensations of trans-piperylene with methyl 3-nitroacrylate and with 3, 3, 3-trichloro-1-nitropropene and the structures of the adducts were established in an analogous way.

In both cases the condensation product, when heated with concentrated sulfuric acid at 100°, was converted into a mixture of m- and o-toluic acids [8]. These were oxidized further with dilute nitric acid in an autoclave under a pressure of 30-40 atm(nitrogen)into a mixture of isophthalic and phthalic acids [9], which were separated by crystallization from water.



From the relative amounts of isophthalic and phthalic acids we established the compositions of the mixtures of products of the condensation of trans-piperylene with methyl 3-nitroacrylate and with 3,3,3-trichloro-1-nitro-propene. In the first case the ortho-meta ratio was 6:1, and in the second case it was 8:1.

Dienophile	ortho-meta ratio	meta-isomer con- tent of product, %
CH <sub>2</sub> = CHNO <sub>2</sub>	only ortho	0
CH <sub>3</sub> CH= CHNO <sub>2</sub>	14:1	6.7
C <sub>6</sub> H <sub>5</sub> CH = CHNO <sub>2</sub>	12:1	8
CC1 <sub>3</sub> CH = CHNO <sub>2</sub>	8:1	11.1
CH <sub>3</sub> OOCCH=CHNO <sub>2</sub>	6:1	14.5

Also, by a freezing treatment on the product of the condensation of trans-piperylene with 3, 3, 3-trichloro-1-nitropropene we obtained two substances in 10:1 proportions, m. p.  $63-64^\circ$  and  $25-27^\circ$  respectively. When heated with concentrated sulfuric acid, each of these was converted into m-toluic acid. It is evident that these two substances were stereoisomers. Hence, in the condensation of 1,2-disubstituted nitro dienophiles with trans-piperylene in all cases a mixture of struc-

turally isomeric adducts (ortho and meta) is formed in which the ortho isomer greatly predominates. Data on the change in the proportion of the meta isomer in the condensation products are given in the table.

The predominant formation of ortho isomers suggests that the nitro group is a much stronger orientant than electron-donor substituents ( $CH_3, C_6H_5$ ) and such electron-acceptor substituents as  $CCl_3$  and  $COOCH_3$ .

From an analysis of the data obtained we may state that in the condensation of trans-piperylene with nitroethylene (RCH = CHNO<sub>2</sub>, R = H) addition goes strictly selectively with formation of the ortho isomer as the sole product. However, on the introduction of electron-donor substituents into the dienophile molecule the structural selectivity of the reaction diminishes and 7-8% of meta isomer is formed. The proportion of meta isomer increases to 11-14.5% on introduction of electron-acceptor groups such as methoxycarbonyl and trichloromethyl into the dienophile.

## EXPERIMENTAL

Structure of the Adduct Obtained from Piperylene and Nitroethylene. 5.6 g of the product of the condensation of piperylene and nitroethylene [1] [b. p. 90-93.5° (8 mm);  $n_D^{20}$  1.4798;  $d_4^{20}$  1.0751] was dissolved in 10 ml of absolute ethanol, and to the resulting solution in an atmosphere of nitrogen at 12° a solution of sodium ethoxide (1.84 g of sodium in 20 ml of absolute ethanol) was added dropwise; the mixture was left overnight at room temperature. The resulting solution of the sodium salt of the adduct was added in the course of five minutes with stirring at 0-4° to a mixture of 18.2 ml of concentrated HC1, 250 ml of water, and 100 ml of acetone. The solution was then stirred at 25° for one hour, 18 ml of concentrated HC1 was added, and the mixture was refluxed for one hour. When the solution had cooled, it was diluted with an equal volume of water and extracted with ether, the extract was washed with water and dried over anhydrous magnesium sulfate, ether was driven off, and the residue was distilled. We obtained 4.0 g (92%) of a ketone having: b. p. 38-39° (2.5 mm) for 175° (744.5 mm);  $n_D^{20}$  1.4872.

The literature [6] gives: b. p. 178-180°;  $n_D^{20}$  1.4831. Semicarbozone, m. p. 208.5-209° (from ethanol). A mixture of the semicarbazone obtained and the semicarbazone of 2-methyl-3-cyclohexene-1-one melted without depression.

We prepared the 2,4-dinitrophenylhydrazone, m. p. 206-206.5° (benzene or ethyl acetate). In chromatography on alumina only one 2,4-dinitrophenylhydrazone of m. p. 206-206.5° was isolated.

<u>Structure of the Adduct Obtained from Piperylene and 1-Nitropropene</u>. 15.5 g of the product of the condensation of piperylene with 1-nitropropene [1] [b. p. 84-85.5° (8 mm);  $n_D^{20}$  1.4719;  $d_4^{20}$  1.0465 ] was hydrogenated in 50 ml of absolute methanol over 0.2 g of Adams platinum catalyst. The theoretical amount of hydrogen (2240 ml at 20° and 760 mm) was absorbed in five hours. After distillation we obtained 12.8 g (about 81%) of a substance having: b. p. 75-76° (5-6 mm);  $n_D^{20}$  1.4606;  $d_4^{20}$  1.0154.

In a stream of nitrogen a solution of sodium ethoxide (2.3 g of sodium in 30 ml of absolute ethanol) was added dropwise to a solution of 8.4 g of the hydrogenation product in 130 ml of absolute ethanol at 15°, and the mixture was left overnight. The resulting solution of the sodium salt of the hydrogenated adduct was added with stirring at 0° to a mixture of 78 ml of concentrated HC1, 780 ml of water, and 500 ml of acetone. The solution was stirred at 25° for one hour and then heated at 45-50° under reflux for one hour. When the solution had cooled, it was diluted with an equal volume of water and extracted with ether. The extract was washed with water and dried over anhydrous sodium sulfate, ether was driven off, and the residue was distilled. We obtained 5.9 g (89%) of a mixture of ketones, b. p. 65-84° (10-11 mm). From 1.3 g of this mixture and 1.04 g of 2, 4-dinitrophenylhydrazine dissolved in a mixture of 26 ml of ethanol, 7.8 ml of water, and 5.2 ml of concentrated H<sub>2</sub>SO<sub>4</sub> we obtained 3 g of a mixture of the corresponding 2, 4-dinitrophenylhydrazones. By successive fractional crystallizations from ethanol and its mixture with ethyl acetate we obtained the 2,4-dinitrophenylhydrazone of 2,6-dimethylcyclohexanone, m. p. 149-150°, and the 2,4-dinitrophenylhydrazone of 2,3-dimethylcyclohexanone, m. p. 112-113°. In admixture with known samples the two isomers melt without depression.

Condensation of Piperylene with  $\beta$ -Nitrostyrene. A mixture of 5.36 g of  $\beta$ -nitrostyrene, 4.7 g of piperylene, and 0.05 g of pyrogallol was heated in a sealed tube for 12 h at 100°. After distillation we obtained 7.8 g (about 63%) of adduct, m. p. 72-79° After successive fractional crystallizations from ethanol and its mixture with petroleum ether we obtained 7.2 g of 3-methyl-4-nitro-5-phenylcyclohexene, m. p. 93-94°, and 0.6 g of 3-methyl-5-nitro-4phenylcyclohexene, m. p. 98-99°. The literature [3] gives: 3-methyl-4-nitro-5-phenylcyclohexene, m. p. 94-95°; 3-methyl-5-nitro-4-phenylcyclohexene, m. p. 98-99°.

Structure of the Adduct Obtained from Piperylene and Methyl 3-Nitroacrylate. 7.9 g of the product of the condensation of piperylene with methyl 3-nitroacrylate [1] [b. p. 108-108.5 (1 mm);  $n_D^{20}$  1.4795;  $d_4^{20}$  1.1819] was added at 0° to 20 ml of concentrated H<sub>2</sub>SO<sub>4</sub> the mixture was heated gradually up to 100°, and heating at this temperature was continued for four hours. The cooled mass was poured onto ice, and the dark-colored crystalline precipitate was filtered off and dissolved in boiling water. The aqueous extract was cooled, and a mixture of toluic acids separated and was dissolved in benzene for the purpose of purification. The benzene solution was evaporated to dryness, and the colorless residue (0.52 g) was oxidized further with 20 ml of 30% nitric acid in an autoclave under a pressure of 30 atm of nitrogen at 200° for three hours to convert it into benzenedicarboxylic acids. At the end of the reaction the nitric acid solution was evaporated to dryness. We obtained 0.105 g of a mixtue of isophthalic (m. p. 347-348°) and phthalic (m. p. 191-192°) acids, which were separated in 6:1 proportions by taking advantage of their different solubilities in hot water. The original adduct was therefore a mixture of methyl 5-methyl-6-nitro-3-cyclohexene-1-carboxylate and methyl 2-methyl-6-nitro-3-cyclohexene-1-carboxylate.

Structure of the Adduct Obtained from Piperylene and 3,3,3-Trichloro-1-nitropropene. 127 g of the unrecrystallized product of the condensation of piperylene with 3,3,3-trichloro-1-nitropropene [1] (m. p. 60-61°) was subjected to successive freezing treatments, as a result of which we isolated a crystalline substance of m. p. 60-61°, which after recrystallization from hexane melted at 63-64° (102 g). By a further freezing treatment on the liquid part at  $-70^{\circ}$  we isolated a low-melting compound, which after recrystallization from petroleum ether melted at 25-27° (10.2 g). To prove the structures of the isomers isolated each of them was heated with concentrated H<sub>2</sub>SO<sub>4</sub>. 14 g of the adduct of m. p. 63-64° was added with stirring to 50 ml of concentrated H<sub>2</sub>SO<sub>4</sub> cooled to 0°. The reaction mixture was gradually warmed to room temperature and then heated for four hours at 100°. The dark-colored reaction mixture was poured onto ice, and the precipitated solid was filtered off and crystallized, first from water and then from petroleum ether. We obtained 0.85 g of m-toluic acid, m. p. 111-112°, undepressed by admixture with a known sample.

The second isomer, m. p. 25-27°, also gave m-toluic acid when heated with concentrated sulfuric acid. It is evident that the substances isolated were stereoisomers of the ortho adduct. We did not prove the structures of the stereoisomers. In order to distinguish the structural isomers the unrecrystallized condensation product (57 g) was heated in the same way with concentrated  $H_2SO_4$ , and we obtained a mixture of o- and m-toluic acids, m. p. 94-99° (2.1 g).

2.1 g of the toluic acids was heated with 10 ml of 30% nitric acid under a pressure of 30 atm of nitrogen at 200° for three hours. The nitric acid solution was evaporated to dryness, and we obtained 1.4 g of a mixture of iso-phthalic and phthalic acids, which were separated in 8:1 proportions by taking advantage of their different solubilities in hot water. The condensation product, therefore, was a mixture of 3-methyl-4-nitro-5-(trichloromethyl)cyclo-hexene and 3-methyl-5-nitro-4-(trichloromethyl)cyclohexene.

## SUMMARY

1. A study was made of structural orientation in the diene condensation of trans-piperylene with the nitro dienophiles RCH = CHNO<sub>2</sub>, in which R = H, CH<sub>3</sub>, C<sub>6</sub>H<sub>5</sub>, CCl<sub>3</sub>, COOCH<sub>3</sub>.

2. In the condensation of trans-piperylene with nitroethylene (R = H) the only reaction product is the ortho isomer.

3. In the condensation of trans-piperylene with 1,2-disubstituted nitro dienophiles ( $R = CH_3$ ,  $C_6H_5$ ,  $CCl_3$ , COOCH<sub>3</sub>) in all cases two structurally isomeric adducts are formed with a great predominance of the ortho isomer.

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