1-ISOPROPYL-3-tert-BUTYL-1,2-DIAZA-1,3-BUTADIENE IN [4 + 2]-CYCLOADDITION REACTIONS

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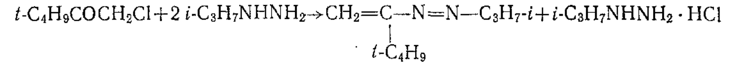
1-Isopropyl-3-tert-butyl-1,2-diaza-1,3-butadiene (I), which is formed as a result of the reaction of α-chloropinacoline with isopropyl hydrazine, exists in the form of a mixture of cisoid and transoid conformations and is extremely active in the diene synthesis with maleic anhydride, maleimide, dimethyl fumarate, and methyl vinyl ketone. The conformations of the derivatives obtained, which contain a Δ^2-tetrahydropyridazine ring, were established on the basis of the PMR spectra. 1-Isopropyl-3-tert-butyl-trans-5,6-dicarbomethoxy-Δ^2-tetrahydropyridazine was obtained from dimethyl fumarate and I; this was confirmed by a comparison of data on it with the characteristics of the cis isomer, synthesized by the action of diazomethane on the anhydride of 1-isopropyl-3-tert-butyl-Δ^2-tetrahydropyridazine-5,6-dicarboxylic acid.

Cisoid dinenes are much more active than transoid dienes in the diene synthesis, and this serves as one of the confirmations of the synchronous mechanism of the Diels–Alder reaction [1]. We have synthesized 1-isopropyl-3-tert-butyl-1,2-diaza-1,3-butadiene (I) via the scheme

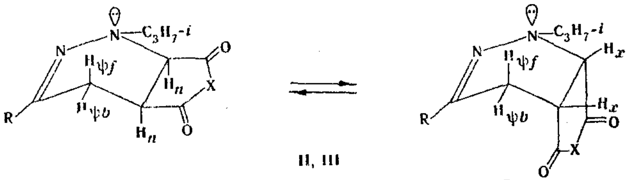


$$t\text{-}C_4H_9COCH_2Cl + 2\ i\text{-}C_3H_7NHNH_2 \rightarrow CH_2{=}\underset{t\text{-}C_4H_9}{\underset{|}{C}}{-}N{=}N{-}C_3H_7\text{-}i + i\text{-}C_3H_7NHNH_2 \cdot HCl$$

Diazabutadiene I is the first representative of aliphatic α,β-unsaturated azo compounds, which exist as a mixture of s-cis and s-trans conformations. This follows from a comparison of its UV spectrum (Fig. 1) with the spectra of the transoid 1-isopropyl-3-methyl-1,2-diaza-1,3-butadiene and the cyclic derivative – 3,3,5-trimethyl-[3H]-pyrazole [2]. The two maxima of the $\pi \rightarrow \pi^*$ transitions at 226 and 255 nm correspond to the transoid and cisoid conformations, respectively.

As one should have expected, diimide I is more active than the other 1,2-diaza-1,3-butadienes [3-5] in 1,4-cycloaddition and gives quantitative yields of the products of the diene synthesis with maleic anhydride and maleimide, even in the cold, and with dimethyl furmarate and methyl vinyl ketone on brief heating. The structure of adducts II-VII (Table 1) was proved by a comparison of their spectral characteristics with the characteristics of previously described compounds [3-5].

It is possible to establish the preferred conformation of the Δ^2-tetrahydropyridazine derivatives from the PMR spectra (Table 2). Adducts II and III may be found in two conformations ($A \rightleftharpoons B$):



A

II, III

B

II X=O, R=t-C₄H₉; III X=NH, R=t-C₄H₉

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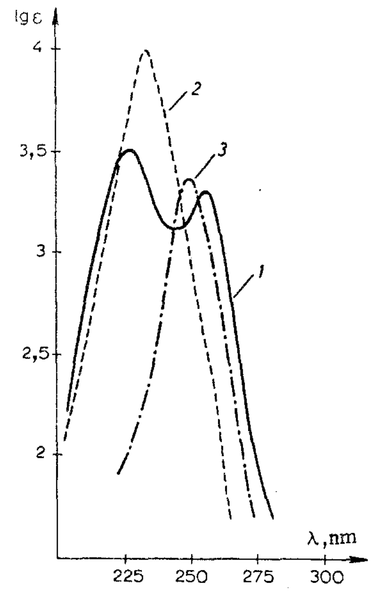
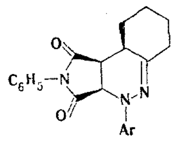


Fig. 1. UV spectra (in n-hexane): 1) 1-isopropyl-3-tert-butyl-1,2-diaza-1,3-butadiene; 2) 1-isopropyl-3-methyl-1,2-diaza-1,3-butadiene; 3) 3,3,5-trimethyl-[3H]-pyrazole.

On the basis of the spin–spin coupling constants of the protons in the 4-6 positions of the ring (ABKX system), the endo conformation (B) should be assumed for II and III. First, the coupling constants of the protons in the 5 and 6 positions correspond to J_{xx}* (9 Hz for II and 10 Hz for III); J_{nn} is usually lower and ranges from 5 to 7 Hz [6, 7]. Second, $J_{\psi b, n}$ is close to zero and does not exceed 2 Hz [6].

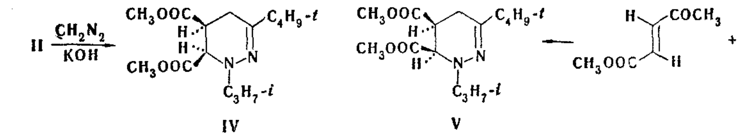
Of the two J_{45} values (9 and 7 Hz), the larger values should be considered to be $J_{\psi f, x}$ [6]; this assignment is also in agreement with the fact that the ψf proton resonates at weaker field than the ψb proton; this is due to the deshielding effect of the unshared electron pair of the $N_{(1)}$ atom, which occupies the ψf position.

Judging from the magnitudes of the constants found, the adducts of arylazocyclohexenes with N-phenylmaleimide [9], for which the constants of coupling of the proton in the 5 position with the protons in the 4 and 6 positions are equal and amount to 9 Hz, are apparently synisomers C.

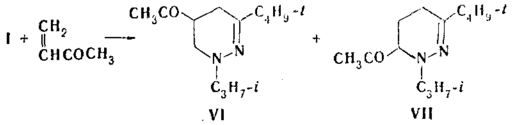


C

It has been shown [5] by means of PMR spectroscopy that in the case of the reaction of dimethyl furmarate with a series of 1,2-diaza-1,3-butadienes, this variant of 1,4-cycloaddition proceeds in accordance with the cis principle [1]. Below we will present the chemical confirmation of this. Treatment of adduct II with diazomethane gives 1-isopropyl-3-tert-butyl-cis-5,6-dicarbomethoxy-Δ^2-tetrahydropyridazine (IV), the ring protons of which form the set of frequencies of an ABKX system in the PMR spectrum, and the coupling constant of the protons in the 5 and 6 positions is 5.5 Hz (J_{ae}). At the same time, isomeric adduct V is obtained as a result of the reaction of I with dimethyl fumarate; this is seen from its PMR spectrum, which also forms an ABKX system in which J_{56} is 7.5 Hz (J_{aa}). Substance V is consequently the trans isomer; this also confirms adherence to the cis principle.



It is interesting to note that in the case of the reaction of I with methyl vinyl ketone, as in other reactions of 1,2-diaza-1,3-butadienes with unsymmetrical dienophiles [3, 4], a mixture of structural isomers (5- and 6-acetyl-Δ^2-tetrahydropyridazines VI and VII) is formed. The structures of the isomers were also established by means of the PMR spectra, from which it follows that the acetyl group in both compounds occupies an equatorial position. The 6-H protons of isomer VI are represented by the AB portion of the ABX system with J_{ae} 2 Hz and J_{aa} 6 Hz; $W_{1/2}$ is 15 Hz for the multiplet of the 6-H proton of isomer VII (the X portion of the ABX system); this is in accord with its axial orientation [10].



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*The following symbols are used: x is exo, n is endo, ψb is quasibowsprit, and ψf is quasiflagpole.

TABLE 1. 1-Isopropyl-3-tert-butyl-Δ^2-tetrahydropyridazines

Compound	d_4^{20}	n_D^{20}	MR_D		Empirical formula	Found, %			Calc., %			$\nu_{C=N}$, cm^{-1}	λ_{max}, nm (ε)	Yield, %
			found	calc.		C	H	N	C	H	N			
II	1,0874	1,4807	66,00	66,39	$C_{13}H_{20}N_2O_3$	62,2 62,1	7,9 8,1	11,3 11,1	61,9	7,9	11,1	1610	250 (5000)	100
III*	—	—	—	—	$C_{13}H_{21}N_3O_2$	62,3 62,4	8,3 8,4	16,6 16,8	62,2	8,4	16,7	1620	—	100
IV	1,0412	1,4700	79,95	79,52	$C_{15}H_{26}N_2O_4$	60,4 60,3	8,6 8,7	9,5 9,6	60,4	8,7	9,6	1640	—	80
V	1,0233	1,4610	80,01	79,52	$C_{15}H_{26}N_2O_4$	60,4 60,6	8,8 8,8	9,7 9,7	60,4	8,7	9,6	1640	—	100
VI	0,9190	1,4642	67,09	66,69	$C_{13}H_{24}N_2O$	69,7 69,8	10,9 11,0	12,4 12,5	69,6	10,7	12,5	1610	240 (7300)	
VII	0,9208	1,4626	67,02	66,69	$C_{13}H_{24}N_2O$	69,9 69,8	11,0 11,1	12,5 12,4	69,6	10,7	12,5	1620	240 (8100)	100

*This compound had mp 116° [from benzene–heptane (1:1)].

TABLE 2. PMR Spectra of II-VII*

Compound	δ, ppm (J, Hz)				
	t-C_4H_9	n-$CH(CH_3)_2$†	4-H	5-H	6-H
II	1,1 s	1,2 d 1,25 d 3,9 sep (7)	2,2 dd ($J_{gem}=15, J_{45}=7$) 2,6 dd ($J_{gem}=15, J_{45}=9$)	3,5 dt ($J'=7, J''=9$)	4,3 d (9)
III	0,9 s	1,1 d 1,2 d 4,3 sep (7)	2,2 dd ($J_{gem}=13, J_{45}=7$) 2,8 dd ($J_{gem}=13, J_{45}=9$)	3,3 ddd ($J'=10, J''=9, J'''=7$)	4,4 d (10)
IV	0,9 s	0,8 d 1,05 d 3,9 sep (7)	2,2—2,8 m	2,9—3,2 m	4,7 d (5,5)
V	1,0 s	0,95 d 1,2 d 3,8 sep (7)	2,2 dd ($J_{gem}=17, J_{45}=7{,}5$) 2,7 dd ($J_{gem}=17, J_{45}=5$)	3,6 dt ($J'=5, J''=7{,}5$)	4,3 d (7,5)
VI	1,15 s	1,1 d 3,4 sep (7)	2,0—2,4 m	2,4—2,8 m	2,9 dd ($J_{gem}=18, J_{45}=6$) 3,1 dd ($J_{gem}=18, J_{56}=2$)
VII	1,1 s	1,0 d 1,25 d 3,2 sep (7)	1,8—2,4 m		3,3 m

*Abbreviations: s is singlet, d is doublet, t is triplet, sep is septet, and m is multiplet.

†The magnetic nonequivalence of the methyl groups of the isopropyl group attached to $N_{(1)}$ for all the 6-X-substituted Δ^2-tetrahydropyridazines is a consequence of their diastereotopic character because of the fact that $C_{(6)}$ is asymmetric [8].

According to gas-liquid chromatography (GLC), the ratio of VI to VII is 2:3. It follows from a comparison with previous results [3, 4] that the fraction of the 5-X-substituted isomer increased when a tert-butyl group was introduced into the 3 position. This is not in agreement with data on the structural orientation for carbodienes, for which the fraction of the meta isomer (5-X-substituted product in our case) falls [1]. The reason for this apparently consists in fine geometrical differences in the two transition states, which lead to two structural isomers, VI and VII.

EXPERIMENTAL

The UV spectra of 10^{-2} and 10^{-4} M solutions, prepared by the method of double dilution, were recorded with an SF-8 spectrometer. The IR spectra of 20-40-μ-thick layers of the liquid preparations and of thin layers of mineral oil suspensions of the solids were obtained with a UR-10 spectrophotometer. The PMR spectra were recorded with a Varian-HA-100 D spectrometer. Hexamethyldisiloxane was used as the internal standard. A Tswett-4M chromatograph with a glass column (2 m long and 3 mm in diameter) packed with polyethylene glycol M 4000 on a TNDM support (70-80 mesh) was used for the GLC analysis. The column temperatures were 80 and 120°, and nitrogen was the carrier gas.

α-Chloropinacoline. A 135-g (1 mole) sample of sulfuryl chloride was added at room temperature to a solution of 100 g (1 mole) of pinacoline in 600 ml of methylene chloride, after which the mixture was allowed to stand for 15 min. The solvent was removed in vacuo (40 mm), and the residue was washed several times with water, 20% $NaHCO_3$ solution, and water, dried with $CaCl_2$, and distilled to give 83.4 g (62%) of chromatographically pure 1-chloro-3,3-dimethyl-2-butanone with bp 67-69° (11 mm), d_4^{20} 1.1273, and n_D^{20} 1.4438 [bp 75-76° (15 mm) and n_D^{20} 1.4422 [11]].

1-Isopropyl-3-tert-butyl-1,2-diaza-1,3-butadiene (I). An 80.7-g (0.6 mole) sample of α-chloropinacoline was added to a solution of 118.4 g (1.2 mole) of isopropylhydrazine in 150 ml of diethyl ether in the presence of 15 g of $CaCl_2$ in the course of 15 min. The mixture was refluxed for 3 h, after which it was cooled, washed with water, and dried with $MgSO_4$. The solvent was removed by distillation to give 37.9 g (41%) of pure (according to GLC) diazabutadiene I with bp 59° (25 mm), d_4^{20} 0.8020, and n_D^{20} 1.4281. Found: C 70.1, 70.0; H 12.0, 12.0; N 18.2, 18.3%; MR_D 49.48. $C_9H_{18}N_2$. Calculated: C 70.1; H 11.8; N 18.2%; MR_D 49.38. IR spectrum, ν, cm^{-1}: 1510 (N=N), 1618 (C=O), 3105 (=C−H). UV spectrum, λ_{max}, nm (ε): in hexane 226 (3400), 255 (2100), 400 (140); in acetonitrile 397 (55). PMR spectrum: δ126 [$C(CH_3)_3$, s], 1.34 [$(CH_3)_2C$, d, J 7 Hz], 3.82 (N−CH, sep, J 7 Hz), 4.35 (β-cis-CH, m), 4.66 (β-trans-CH, m).

1-Isopropyl-3-tert-butyl-Δ^2-tetrahydropyridazine-5,6-dicarboxylic Acid Anhydride (II). A solution of 3.3 g (0.022 mole) of I and 2.33 g (0.023 mole) of maleic anhydride in 30 ml of benzene was held at room temperature for 50 h, after which the solvent was removed in vacuo, and the residue (a viscous oil) was dissolved in hexane. The solution was filtered to remove traces of maleic anhydride, and the filtrate was dried with $MgSO_4$. The solvent was removed in vacuo to give 5.0 g (100%) of anhydride II.

1-Isopropyl-3-tert-butyl-Δ^2-tetrahydropyridazine-5,6-dicarboxylic Acid Imide (III). A solution of 3.3 g (0.022 mole) of I and 2 g (0.02 mole) of maleimide in 100 ml of methylene chloride was held at room temperature for 100 h, after which the solvent was removed in vacuo, and the residue was recrystallized from benzene−heptane (1:1) to give 5.0 g (100%) of imide III.

1-Isopropyl-3-tert-butyl-cis-5,6-dicarbomethoxy-Δ^2-tetrahydropyridazine (IV). A solution of 1.61 g (0.024 mole) of diazomethane [12] in 30 ml of diethyl ether was added in the course of 20 min to a mixture of 3 g (0.012 mole) of II and 4 ml of 10% KOH, after which the mixture was allowed to stand for another 4 h. The organic layer was separated and dried with $MgSO_4$. The solvent was removed, and the residue was chromatographed on Al_2O_3 (activity III) with elution by ether−ethyl acetate (3:1) to give 2.84 g (80%) of pure (according to TLC) tetrahydropyridazine IV.

1-Isopropyl-3-tert-butyl-trans-5,6-dicarbomethoxy-Δ^2-tetrahydropyridazine (V). A mixture of 2.16 g (0.015 mole) of dimethyl fumarate and 3.1 g (0.015 mole) of I in 25 ml of benzene was heated at 60° for 100 h. The solvent and volatile components were removed in vacuo, and the residue (4.5 g), which, according to TLC, consisted of primarily one substance, was purifed by passage through a column filled with Al_2O_3 (activity III) with elution by petroleum ether−ethyl acetate (3:1) to give 4.4 g (100%) of pure (according to TLC) tetrahydropyridazine V.

1-Isopropyl-3-tert-butyl-5- and 6-Acetyl-Δ^2-tetrahydropyridazines (VI and VII). A mixture of 5.4 g (0.035 mole) of I and 3.1 g (0.044 mole) of methyl vinyl ketone was heated in a sealed ampul at 60° for 50 h. The volatile components were removed in vacuo, and the residue [7.85 g (100%)] was, according to GLC, a mixture of structural isomers (VI and VII) in a ratio of 39:61. The isomers were separated with a column filled with Al_2O_3 (activity III) with elution by petroleum ether−diethyl ether (2:1). A 3.1 g sample of the mixture yielded 0.9 g of VI and 2.1 g of VII.

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