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STEREOCHEMISTRY OF THE SYNTHESIS OF 1,2,3,4-TETRAHYDROCINNOLINES FROM ARYLDIAZENIUM SALTS AND OLEFINS

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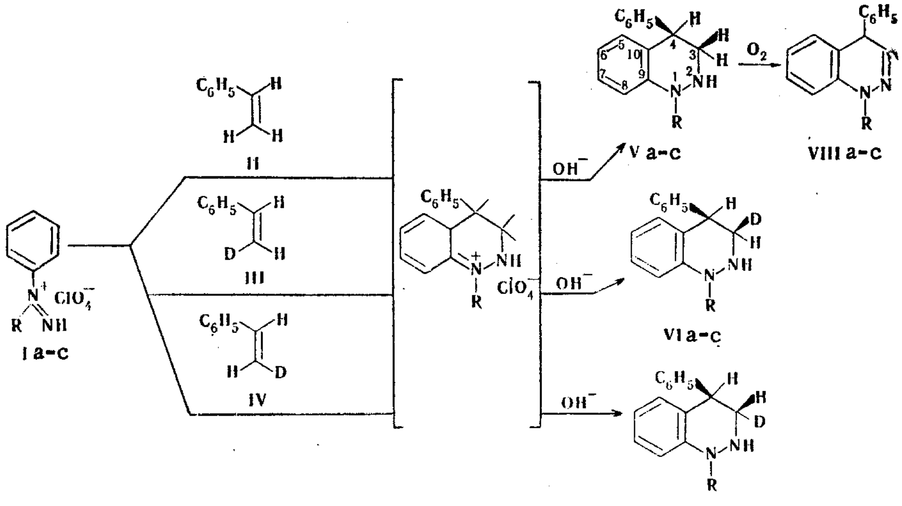
It follows from the PMR spectra that the reaction of 1-methyl-, 1-phenyl-, 1-ethyl-, 1-phenyl-, and 1,1-diphenyldiazenium salts with cis- and trans-d-styrenes, which leads to the corresponding 3-d-4-phenyl-1,2,3,4-tetrahydrocinnolines, takes place with retention of the configuration in the starting styrenes. It is therefore proposed that this reaction be regarded as a special case of $[4^{+}\pi_{s} + 2\pi_{s}]$-cycloaddition.

A new and promising method for the synthesis of cinnoline derivatives was recently proposed [1, 2]; this method consists in the reaction of nucleophilic alkenes with diazenium salts. An unconfirmed mechanism with the participation of intermediate ionic particles in which the (1-C)—(9-C) and (4-C)—(10-C) bonds are formed separately and the reaction is consequently nonstereospecific, was adopted for this transformation [2]. However, this trans-



I, V-VIII a R = CH_3; b R = C_2H_5; c R = C_6H_5

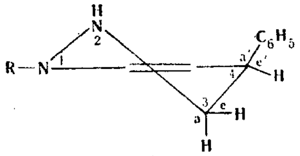


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TABLE 1. Characteristics of 1,2,3,4-Tetrahydrocinnolines (V-VII) and 1,4-Dihydrocinnolines (VIII)

Compound	R_f	IR spectrum, cm^{-1}		UV spectrum		Parameters of the PMR spectrum, δ, ppm (J, Hz)		Yield, %
		C=N	NH	λ_{max}, nm	lg ε	3-H	4-H	
Va[2]	0,43	—	3180	299 254	3,55 3,91	ax 2,94 dd (13,8, 5,2)[a] eq 3,22 dd (13,8, 5,2)	3,95 t (5,2)	60
Vb	0,6	—	3180	299 254	3,40 3,71	ax 3,00 dd (13,8, 4,2) eq 3,21 dd (13,8, 5,1)	3,96 dd (4,2, 5,1)	50
Vc[2]	0,6	—	3320	291	4,18	ax 2,99 dd (13,8, 6,0) eq 3,29 dd (13,8, 6,0)	3,98 t[b] (6,0)	90
VIa	0,43	—	3180	299 254	3,55 3,91	eq 3,23 d (5,5) c	3,91 d (5,5)	60
VIb	0,6	—	3180	299 254	3,40 3,71	eq 3,30 d (5,1) c	3,72 d (4,8)	45
VIc	0,6	—	3320	291	4,18	eq 3,25 d (6,0) c	3,88 d (6,0)	95
VIIa	0,43	—	3180	299 254	3,55 3,91	ax 3,00 d (5,2) c	3,95 d (4,5)	50
VIIb	0,6	—	3180	299 254	3,40 3,71	ax 2,96 d (4,2) c	3,74 d (4,2)	50
VIIc	0,6	—	3320	291	4,18	ax 2,88 d (6,0) c	3,83 d (6,0)	95
VIIIa	0,7	1600	—	303 230	3,55 3,75	6,55 d (2,8)	4,30 d (2,8)	90
VIIIb	0,8	1600	—	303 230	3,07 3,48	6,55 d (2,4)	4,35 d (2,4)	85
VIIIc	0,8	1600	—	280	4,10	6,58 d (3,0)	4,37 d (3,0)	80

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a) According to the data in [1], the 3-H multiplet is found at 3.05-3.40 ppm (2H) and the 4-H triplet is found at 3.95 ppm (1H). b) From [1]: ABX system, δ_A 3.38, δ_B 3.10, δ_X 4.08 ppm, J_{AB} 7.0, J_{AX} 3.15, and J_{BX} 2.85 Hz. c) The components of the doublet are appreciably broadened due to geminal interaction with the deuteron.

formation can be classified as a concerted reaction by regarding it as polar 1,4-cycloaddition in which the olefin is a dienophile and the diazenium cation is a diene component. Reactions of this type are characteristic for acridizinium [3], acylimmonium [4], and thioacylimmonium [5] salts. They are distinguished by their high degree of regiospecificity and stereospecificity, and one should also expect the same in the case under discussion.

To verify this assumption we reinvestigated the reaction of aryldiazenium salts Ia-c with styrene and extended it to cis- and trans-d-styrenes. As a result, we isolated adducts V-VII (Table 1). Their IR spectra contain the absorption of an NH group, and the set of signals in the PMR spectra corresponds to the assigned structure. In addition to the aromatic multiplet of the corresponding intensity at 6.4-7.3 ppm in the spectra of products Va-b and VIIa-b obtained from methyl- and ethylphenyldiazenium cations, one also observes corresponding signals of 1-N alkyl groups: the CH_3 singlet at 3.0 ppm for Va and VIIa and the CH_2 signal from an ethyl group at 3.4 ppm for Vb and VIIb. The instance of magnetic nonequivalence of the methylene protons of the ethyl group, which is due to the asymmetry of the molecule, is interesting. As a consequence of this, its signal in the spectra of Vb and VIIb is represented by the AB portion of the ABX_3 system ($\Delta\nu$ = 13.5, J_{AB} = 13.8, and $J_{AX} = J_{BX}$ = 6.9 Hz). The NH signal lies at 3.6 ppm and vanishes when D_2O is added. The signals of the 3-H and 4-H protons are given in Table 1. We note the disagreement between our data for Vc and the literature data [1] for the signals of the protons in the 3 and 4 positions. In our case (recording at 270 MHz) this portion of the spectrum is represented by an AMX system (Fig. 1), and its interpretation does not present any difficulties, in contrast to [1], in which the interpretation of the ABX system is evidently incorrect.

The structure of V is confirmed chemically by their easy oxidation to the corresponding 1,4-dihydrocinnolines VIII (Table 1), which differ from the starting tetrahydro derivatives

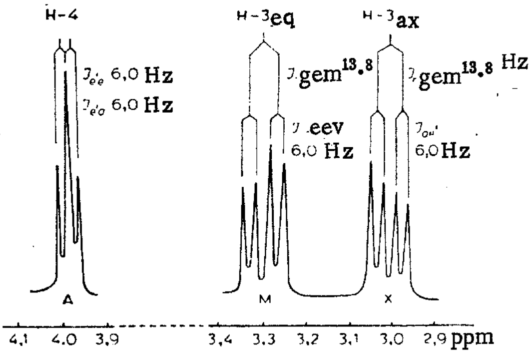

Fig. 1. Fragment of the PMR spectrum of Vc.

with respect to their high chromatographic mobilities. The NH absorption in the IR spectra and the signal of this proton in the PMR spectra vanish on passing from V to VIII, and a new band of a C=N bond appears in the IR spectra. A substantial weak-field shift of the signals of the 3-H and 4-H protons (particularly the 3-H proton) and an appreciable decrease in the spin—spin coupling constant (SSCC) to the values characteristic for 1,4-dihydro structures are observed in the PMR spectra. The signals of the 1-N alkyl substituents also undergo a weak-field shift (the CH_3 singlet for VIIIa is found at 3.35 ppm, and the multiplet of the methylene group attached to 1-N in VIIIb is found at 3.83 ppm). The diastereotopy of the methylene group in the ethyl substituent attached to 1-N is retained ($\Delta\nu$ = 13.5, J_{AB} = 13.8, and J_{AX} = J_{BX} = 6.9 Hz). The V → VIII dehydrogenation definitely expands the preparative possibilities of the investigated cyclocondensation and also serves as unambiguous evidence for its regiospecificity, since the character of the PMR spectrum in the region of the resonance of the protons in the 3 and 4 positions should be completely different in the case of some other type of interlinking.

In the monotypic PMR spectra of 1,2,3,4-tetrahydrocinnolines Va-c synthesized from styrene one's attention is drawn to the high SSCC ($\leqslant$6 Hz) for the protons in the 3 and 4 positions (Table 1). This indicates predominance in these compounds of conformation A with a pseudoequatorial orientation of the 4-H proton; this is a consequence of the $A_{1,2}$ strain [6] that exists between the 5-H hydrogen atom and the phenyl ring in the 4 position.

The doublet of the equatorial 3-H atom is retained in the PMR spectra on passing to cinnoline derivatives VIa-b synthesized from cis-d-styrene, whereas only a stronger-field 3-H_{ax} signal is present in the spectra of VIIa,b obtained from trans-d-styrene. Thus the investigated transformation is stereospecific, and adducts VIa-c with an ae' orientation of the protons in the 3 and 4 positions (the cis isomer) are formed from cis-d-styrene, whereas adducts VIIa-c with an ee' orientation (the trans isomer) are formed with trans-d-styrene. Consequently, the configuration of the starting styrene is retained completely during the reaction.*

The results very likely indicate a concerted mechanism for this reaction, and by virtue of the cationic character of the diene component it can be classified as a diene synthesis with reverse reactivity, i.e., it can be regarded as $[4^+\pi_s + 2\pi_s]$-cycloaddition. In this case 1,4-cycloaddition with diazenium salts is a special case of the azadiene synthesis [7] with the C=C-N=N heterodiene system, which was first observed and investigated in detail in our laboratory [8, 9].

Thus the use of diazenium salts opens up new synthetic possibilities: 1,1-dialkyldiazenium cations are used as dienophiles in the synthesis of pyridazine derivatives [10], and aryldiazenium salts are used as diene components in the synthesis of cinnoline structures.

EXPERIMENTAL

The IR spectra of thin layers of the liquid compounds and 10% solutions of the solid compounds in CCl_4 were recorded with a UR-10 spectrometer. The UV spectra of 10^{-4}-10^{-5} M solutions of the compounds in acetonitrile were recorded with an SF-8 spectrophotometer. The PMR spectra of 10% solutions of the compounds in CCl_4 were recorded with a Bruker HX-270 spectrometer (270 MHz) at 35°C with tetramethylsilane as the internal standard. The purity

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*Signals of stereoisomeric impurities were not detected in the PMR spectra.

of the compounds was monitored by thin-layer chromatography (TLC) on activity IV Al_2O_3 with elution by pentane—ether (4:1) (see Table 1). The reaction products were isolated in the same systems with chromatographic columns.

Spectrally pure acetonitrile was prepared by the method in [11]. The perchloric acid (70%) was purified by vacuum distillation. The lithium perchlorate was recrystallized repeatedly from dioxane and was dried in vacuo at 150°C. The starting 1-methyl-, 1-phenyl- [12], 1-ethyl-, 1-phenyl- [13], and 1,1-diphenylhydrazine [14] were distilled repeatedly under high vacuum conditions (10^{-2} mm) with a column with an efficiency of five theoretical plates. Their purity was monitored by gas—liquid chromatography (GLC) with a Tsvet-4 chromatograph with a glass column (2 m by 2.5 mm) filled with a 15% mixture of Apiezon L (73%), tripropionitrileamine (21.5%), Carbowax 20M (5%), and polyethylenepolyamine (0.5%) on Chromosorb W. The carrier-gas (nitrogen) flow rate was 90 ml/min, and the temperature was 140-160°C. The cis- and trans-d-styrenes [15] were obtained and purified in 40-50% yields. Stereoisomer impurities were not detected from the PMR spectral data (5% accuracy).

1,2,3,4-Tetrahydrocinnolines V-VII. A 5-mmole sample of the corresponding hydrazine was oxidized in 100 ml of a 0.1 M solution of $LiClO_4$ in acetonitrile in the presence of 5 mmole of $HClO_4$ at 0°C. The solution was first flushed with argon for 20 min. The oxidation was carried out in an argon atmosphere at a controllable potential (1.4 V) on a platinum anode (Ag/Ag^+ 10^{-2} M) in an electrochemical cell [16] with a P-5827M potentiostat. The electrolysis was complete after 95% conversion of the hydrazine to the corresponding diazenium salt, as judged from the UV spectroscopic data [2]. UV spectrum of the previously undescribed 1-ethyl-1-phenyldiazenium perchlorate: λ_{max} 315 nm (log ε 3.67).

A 6-mmole sample of the appropriate styrene was added to a solution of the salt, and the mixture was allowed to stand overnight under argon. It was then neutralized with K_2CO_3 and filtered, and 95% of the acetonitrile was removed by vacuum evaporation. The residue was treated with 50 ml of H_2O and extracted with ether (three 50-ml portions). The ether extract was dried over $CaCl_2$ and concentrated in vacuo. The residual oil was purified by chromatography.

1,4-Dihydrocinnolines VIII. Oxygen was bubbled through a solution of 0.5 g of the corresponding V in 20 ml of ether for 24 h, after which the ether was removed, and the residue was chromatographed.

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