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ACYCLIC ISOPRENOID 1,3-DIENEAMINES IN THE DIELS-ALDER REACTION

A. G. Nigmatov and É. P. Serebryakov

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The dieneamines obtained from 3-methyl-2-butenal and citral (Ia) and (Ib, c) enter into [4 + 2]-cycloaddition with monoethyl citrylidenemalonate (II) and prenylidenemalonate (III), respectively, forming the esters of substituted 1,3cyclohexadiene-l-carboxylic acids with side chains of the isoprenoid type. The same or analogous cyclohexadiene can be obtained from "citral dieneamine" (Ib, c) and typical dienophiles (methyl acrylate, diethyl fumarate, etc.) in a two-stage path, including the initial production of derivatives of 2-amino-3-cyclohexene-1-carboxylic acid in the Diels-Alder reaction and then elimination of the amino group from the cyclic adducts. The isomeric composition of the mixture of cyclic adducts formed in the reaction of (Ib + Ic) with diethyl fumarate under strictly aprotic conditions correlates with the ratio of the structural isomers with a Δ^3 and $\Delta^{3(9)}$ bond (Ib, c) in the "citral dieneamine." In the reaction of the dieneamine with the less reactive methyl acrylate the obtained mixture of cyclic adducts contains a significantly larger fraction of the isomer corresponding to the minor $\Delta^{3(9)}$ isomer of the dieneamine.

In the previous communication [1] we showed that the alicyclic 1,3-dieneamines obtained from 3-methyl-2-butenal ["prenal (Ia)] and citral [a three-component mixture of the E/Z isomers with the Δ^3 bond E/Z-(Ib) and with the $\Delta^{3(9)}$ bond (Ic), containing ~4% of the latter] react with the monoethyl esters of prenylidenemalonic (III) and citrylidenemalonic (II) acids under mild conditions, forming derivatives of 1,3-cyclohexadiene-1-carboxylic acid (CHDC) with side chains of the isoprenoid type. Since the obtained compounds are structurally similar to certain pharmacologically active compounds of the 4-(norpolyprenyl)benzoic acid type (see the review [2]), we decided to investigate the reactions of the dieneamines (Ia) and (Ib, c) with α,β -unsaturated esters in greater detail.

[4 + 2]-Cycloaddition to Alkenylidenemalonic Esters. The "crossed" [4 + 2]-cycloaddition reaction between the prenal dieneamine (Ia) and citrylidenemalonic monoester (II) and between the citral dieneamine (Ib, c) and the prenylidenemalonic monoester (III) takes place readily at 20-25°C with spontaneous elimination of the amine molecule and CO_2 . In the first case ethyl 4-methyl-6-(2',6'-dimethyl-1',5'-heptadienyl)-1,3-cyclohexadiene-1-carboxylate (IV) (a mixture of the 1'E and 1'Z isomers in a ratio of ~5:3) is formed with a yield of 63% after 10 min. In the second case a three-component mixture containing the 5,6-cis and 5,6trans stereoisomers of the ester (V), corresponding to addition of the E- and Z-dieneamines of structural type (Ib), and the ester (VI), corresponding to addition of the minor dieneamine (Ic), is formed. The overall yield of the esters (V) and (VI) amounts to 55% (20°C, 1 h) or 69% (80°C, 10 min (Scheme 1).

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It is noteworthy that the ratio of the isomers (V) and (VI) in the obtained mixture of cyclic adducts amounts to ~37:63 (at 20°C) or ~40:60 (at 80°C), whereas the ratio of the isomers corresponding to these cyclic adducts in the initial dieneamine with structures (Ib) and (Ic) is ~96:4 (see [1]). A similar result was obtained in the reaction of the "citral dieneamine" with the monoester (II); the fraction of the products corresponding to the isomer (Ic) was significantly larger than the fraction of (Ic) itself in the dieneamine [1].

The mixture of aminodiesters (VIII) and (IX), obtained with a yield of 57% in the reaction of the dieneamine [(Ib):(Ic) \approx 96:4] with the diester (VII) under mild conditions (20-25°C, 8 days), is converted when heated under vacuum (130°C, 0.02 mm Hg) into a mixture containing ~65 mole % of the initial dienophile (VII), ~30-35% of the aminoester (IX), and only traces of the isomeric aminoester (VIII) and the initial dieneamine (Ib, c). Such a result is evidently due to the smaller steric hindrance and to the greater thermal stability of the cyclic adduct (IX), whereas its more hindered isomer (VIII) readily undergoes retrodiene dissociation to the diester (VII) and the relatively volatile dieneamine (Ib, c). Partial saponification of the enriched aminodiester (IX) with one equivalent of potassium hydroxide in ethanol, acidification of the obtained amino acid salt to pH 7, and sublimation of the reaction product lead to a mixture of the cyclohexadiene esters with the isomers in the ratio (V):(VI) = 9:91. Analysis of this mixture by GLC, PMR spectroscopy, and chromato-mass spectrometry* showed that the ester (V) in the sample of this origin is the pure 5,6-trans isomer, whereas in the analogous sample, produced in a single stage during the reaction of (Ib, c) with the monoester (III), trans-(V):cis-(V):(VI) \approx 14:23:63.

Addition to Typical Dienophiles. The reaction of 1-diethylamino-1,3-butadine (the "crotonaldehyde dieneamine") (X) with typical dienophiles of the $H_2C=CHX$ (where X = CHO, COMe, COOEt, CN), which leads to the corresponding functionally 1-substituted 2-diethylamino-3cyclohexenes, has been known for more than 40 years [3, 4]. The transition from the aminocyclohexenes obtained in this way to functionally 1-substituted 1,3-cyclohexadienes is realized during thermolysis or under the influence of acids [4]. We used the reaction of the

^{*}The determination of the structures and stereochemistry of the obtained compounds in conjugation with the spectral and chromatographic characteristics is discussed at the end of this section.

"citral dieneamine" [(Ib):(Ic) = 96:4] with methyl acrylate (MAC) for the production of the derivatives of cyclohexadienecarboxylic acid with a prenyl or homoprenyl side chain.



The reaction of the mixture (Ib) + (Ic) with methyl acrylate $(20^{\circ}C, 144 \text{ h})$ leads to a 75% yield of a mixture of isomeric aminoesters $(XI):(XII) \sim 2:1$, and the signals from the minor component correspond to structure (XII), formed from the minor component in the "citral dieneamine" (Ic). Thus, in this case too the fraction of the cyclic adduct formed from (Ic) is appreciably higher, while the fraction of the cyclic adduct (XI) formed from E/Z-(Ib) is accordingly lower than the ratio of the components (Ib) and (Ic) in the initial dieneamine.

Thermolysis of the mixture of aminoesters (XI) + (XII) in xylene (~140°C, 32 h) led with a high yield to the required diene esters (XIII) and (XIV). According to data from the PMR spectrum and GLC-MS analysis, the ratio of the isomers (XIII) and (XIV) in the thermolysis product amounts to ~2:1, and in addition ~4 wt. % of the thermolysis product corresponds to the product from their fragmentation-aromatization, i.e., methyl p-toluate (XVa).

It should be noted that the thermolysis of the aminoesters in xylene is preferred to the previously recommended [4] thermolysis in benzyl alcohol, since the transesterification products, i.e., the corresponding benzyl esters, are formed in a large amount (up to 60 wt. % of the thermolysis product) together with the esters (XIII, XIV, XVa) when the mixture (XI) + (XII) is heated in benzyl alcohol. During thermolysis according to [4] (151°C, 4 h) the aminoester (XVI) obtained similarly from the dieneamine (X) and methyl acrylate gave a 64% TABLE 1. Degree of Deuterohydrogen Exchange at the sp²-Hybridized Carbon Atoms in the Dieneamines (Ib) and (Ic) According to Data from the PMR Spectra of Their Mixture*



		∆ ^{3.} -Isomer ((Ib)	Δ ³⁽⁹⁾ -Isomer (Ic)					
Donor of D	C²	C4	C°	C²	C'	Cª			
D₂O CD₃OD	~ 0 50	~10 50	$^{\sim 20}_{\sim 60}$	~100 ~100	$^{\sim 20}_{\sim 60}$	56 70			

*The figures in the table indicate the percentage decrease of the integral intensity of the respective signals compared with their intensity in the initial sample.

yield of a mixture of methyl cyclohexadienecarboxylate (XVII), methyl benzoate (XVb), and the products from their transesterification with benzyl alcohol (Scheme 2).

Since the monoester (III), diester (VII), and methyl acrylate are not the most active dienophiles, the inconsistency between the low $(\sim 4\%)$ content of the isomer (Ic) in the "citral dieneamine" and the significant or even predominant content of the corresponding isomers in the mixtures of cyclic adducts (V) + (VI), (VIII) + (IX), (XI) + (XII), and (XIII) + (XIV) probably indicates rapid interconversion of the isomers (Ib) and (Ic) under the conditions of the Diels-Alder reaction. This suggestion also agrees with the results from cycloaddition of the "citral dieneamine" to dimethyl fumarate (DMF), diethyl fumarate (DEF), and dimethyl maleate (DMM). Under strictly anhydrous conditions the reaction of the mixture (Ib + Ic) in diethyl fumarate in absolute benzene in a thoroughly airtight vessel (20°C, 3 h) gives a mixture of the cyclic aminodiesters (XVIIIa) and (XIXa) in a ratio of ~92:8. In nonabsolute benzene the reaction of the mixture (Ib, c) with diethyl fumarate, with the even more reactive dimethyl fumarate (20°C, 30 min), and with dimethyl maleate (20°C, 120 h) gives a mixture of the cyclic adducts (XVIIIb) and (XIXb) in an identical ratio of ~45:55, respectively.* It is clear that the component (Ic) as sterically less hindered reacts more quickly than E-(Ib) and Z-(Ib), but its decrease is made up as a result of rapid interconversion E/Z-(Ib) \neq (Ic).

In the absence of external factors the facile interconversion (Ib) \neq (Ic) could in principle be realized as thermal [1,3]-antarafacial sigmatropic shift of a hydrogen atom from the C⁹ atom to the C⁴ atom and back. However, the strain of the transition state makes this process unlikely (see [7]). It is more likely that the interconversion (Ib) \neq (Ic) is initiated by traces of proton-donating agents, which attack the molecules of the 1,3-dieneamines preferentially at the δ position with the formation of the conjugated eniminium ions (E/Z-EII) or at the N atom with the formation of N-protonated dieneamine ions (DAI-1 and DAI-2), capable of facile [1,5]-suprafacial shift of hydrogen (see [8, 9]) (Scheme 3).



*According to the PMR spectra, compounds (XVIIIb) and (XIXb) represent mixtures of stereoisomeric adducts with identical composition. Analogous results were noted earlier in the reactions of dimethyl fumarate and dimethyl maleate with enamines [5, 6]. TABLE 2. Degree of Deuteration and the Distribution of the Isotopic Label in the Products from Addition of the "Citral Dieneamine" (Ib):(Ic) = 96:4 to O-Deuterated Monoethyl Prenylidenemalonate (III)-d, Determined by GLC-MS^a



Structure	Content in	Is	Overall deu-			
of adducts	mixture, wt. %	do	d ₁	d2	d3	index, ^b ID
E-(V)-d Z-(V)-d (VI)-d	23,4 25,2 51,4	46,0 51,8 38,0	42,5 45,0 41,3	9,5 2,1 18,0	2,0 1,1 2,7	0,158 0,132 0,44

^aThe intensities of the molecular ions M^+ , $[M + 1]^+$, $[M + 2]^+$, $[M + 3]^+$ were calculated with allowance for the natural abundance of the ²H and ¹³C isotopes for each molecular mass. ^bThe ID index indicates the fraction of the D atom introduced with the monoester (III)-d and entering the molecules of the

cyclic adducts: $D = \frac{m_1^i + 2m_2^i + 3m_3^i}{100} \frac{C^i}{100}$, where m_1^i , m_2^i , and m_3^i are the fractions of the mono-, di-, and trideuterated cyclic adducts (wt. %), and C^i is the fraction of the given isomer in the mixture of cyclic adducts (wt. %).

The fact that even traces of atmospheric moisture can act as such a proton-donating agent can be seen from the following observations.

1. In the reaction of the mixture (Ib, c) with diethyl fumarate the ratio of the isomeric cyclic adducts (XVIII):(XIX) varies from 92:8 to 45:55 if the reaction vessel is not airtight.

2. In the reaction of the dry freshly distilled mixture (Ib, c) with dry freshly distilled methyl acrylate in absolute benzene (in a closed vessel) followed by thermolysis of the native mixture of cyclic adducts (XI) + (XII) in xylene a mixture of diene esters, in which the ratio of (XIII) + (XIV) is ~2:1, is formed. If the vessel is then made airtight, this ratio changes reliably to (XI):(XII) = 3:1, which indicates retardation of the interconversion (Ib) \neq (Ic).

3. In the absence of moisture (or of the citral impurity) the freshly prepared mixture of the dieneamines (Ib) + (Ic) keeps a constant composition (Ib):(Ic) = 96:4 for at least 48 h at 20°C (PMR). During deuterohydrogen exchange in CD_3OD , which takes place with partial transformation of the mixture (Ib, c) to the solvolysis products (see below), the obtained mixture of deuterated derivatives (Ib) and (Ic) after isolation and purification by distillation under anhydrous conditions has the composition (Ib)-d:(Ic)-d = 70:30, which does not change during storage (20°C, 48 h).

4. During deuterohydrogen exchange in the mixture of dieneamines (Ib, c) with D_2O or CD_3OD the degree of deuteration of the minor component (Ic) is higher than the degree of deuteration of (Ib). This indicates that exchange by the path (Ic) \neq [DAI-2] \neq [E/Z-EII] \neq (Ic) takes place at a higher rate than exchange in (Ib), i.e., the predominant component in the mixture of dieneamines (Table 1).

5. During cycloaddition of the "citral dieneamine" [(Ib):(Ic) = 96:4] to the O-deuterated monoester of prenylidenemalonic acid (III)-d in absolute benzene (80°C, 1 h) a mixture of undeuterated diene esters (E-V), Z-(V), and (VI) with their mono-, di-, and tri-deuterated analogs, subsequently denoted as E/Z-(V)-d + (VI)-d, was obtained. Its composition and the distribution of the isotopic label in the isomeric esters E-(V)-d, Z-(V)-d, and (VI)-d conPMR Spectra (250 MHz) of Derivatives of Cyclohexadienecarboxylic Acid with Isoprenoid Side Chains TABLE 3.







Mixture of iso-			δ,	ppm (integral	intensity)					
meric cyclic adduct (ratio according to GLC)	2- <u>H</u> a	3- <u>H</u> a	4-Me	4a and 4b <u>H</u> .	p.H.b	2 ^{-H} c	p-q ^{H-9}	pH-'1	2′-Me	Other ^e
1'E-(IV)/1'Z-(IV) == 62:38	6,98 d (>0,5 H) (,97 d (>0,5 H)	5,81d.d (111)	1,84 s (3H)	1	$2,56 m \sim 1,9$ ($\sim 0,6$) 2,41 m ($\sim 0,4$) ($\sim 0,4$)	96 df H) H)	3,55 b-d d.d.d	5,18 br.d (111)	1,57 s (1,8 H) 1,70 s (1,2 H)	1,64 s (4,2 H) 1,72 s (1,8 H) 5.03 br.t (0,6 H) 5,16 m (0,4 H)
(X111)/(X1V) = 67:33	6,98 d (~0,67 H) (,~0,33 H) (~0,33 H)	5,85 m (1H)	1,92 s (2H)	2,2 br.sf	2,3-2,5	۔۔۔۔۔ ۲۰۰	2,32,9 mf			1,55s (2 H) 1,64s (1 H) 1,70s (3 H) 5,12m (1 H)
<pre>trans-(V) :cis-(V) : : (V1)=14:23:63</pre>	6,98 d (0,15 H) 6,92 d (0,25 H) 7,00 d (~0,6 H)	5,8 m (1H)	1,87 s (~0.4 H) 1,89 s (~0,7 H)	2.15 br.s ^f (2,511)	2,56m 2 (0,6 H) (- 2,1-2,4 (~1,2	2,06 mf ~0.6 H) H)	3,78 dc, d (0,15 11) 3,5 d, d ^b , d (0,25 11) 3,56d d, d ^b , d ($\sim 0,6$ 11)	5,18 br.d (111)	1,56 s (1,2 H) 1,02 s (1,8 H) 1,68 s (1,2 H) 1,68 s (1,2 H) 1,70 s (1,8 H)	1,65 s (1,8 H) 1,72 s (2,4 H) 1,75 s (1,8 H) 5,10 m (1 H)
3.1 - 6 Uc	- ,								-	

 $b_{J_5}^{\alpha J_2}(\beta), \epsilon$ from 8.6 ± 0.1 Hz (IV), (VI) to 5 Hz cis-(V) ($J_{\alpha\beta} \sim 17.5$ Hz). $b_{J_5}^{\sigma J_5}(\beta), \epsilon$ from 1.6 ± 0.2 Hz (IV), (VI) to ~0 Hz trans-(V). $d_{J_6,1}^{J_6}(1) = 10$ Hz [7 Hz for trans-(V)].

 e Allyl -CH₂ units ($\delta \sim 2.0-2.5$ ppm, m), alkoxyl groups at $\delta 3.7$ s (3H) for (XIII) and (XIV) or 1.25-1.28 t (3H) + 3.95-4.10 q (2H).

fpartial overlap with the multiplets of the allyl CH₂ groups.

firm that the intensity of deuterohydrogen exchange in the dieneamine isomers varies similarly to the rate of their cycloaddition to the monoester (III)-d; the degree of deuteration of the minor dieneamine (Ic) is higher than that of E-(Ib) and Z-(Ib), while the cyclic adduct (VI)-d formed from (Ic) and (III)-d predominates in the mixture of diene esters (Table 2).

Our results show that acyclic isoprenoid 1,3-dieneamines, beginning with "citral dieneamine," can react with dienophiles in two structurally isomeric forms. On account of the equilibrium between these two forms, which is quickly established in the presence of protondonating agents, the composition of the mixture of cyclic adducts can differ significantly from the isomeric composition of the original dieneamine with an increase in the proportion of structures of type (VI), (XII), (XIV), and (XIX).

<u>PMR Spectra and the Data from GLC-MS Analysis.</u> Earlier [10] we interpreted the composition of a six-component mixture of geometric isomers and stereoisomers of derivatives of cyclohexadienecarboxylic acid having structures (XX) and (XXI) by comparison of the data from GLC and GLC-MS analysis of this mixture with data from its PMR spectrum (at 250 MHz); the assignments were confirmed by the correpsonding analysis of the four-component mixture of aromatization products.



The reference for interpretation of the PMR spectrum of the mixture (XX) + (XXI) was the spectrum of the disubstituted diene ester (XXII) synthesized according to [10]. The structures of the cyclohexadienecarboxylic acid derivatives obtained in the present work and the composition of the mixtures were determined in the same way.

Thus, according to GLC analysis the ester (IV) consists of two isomers with R_t 9.02 and 9.15 min in a ratio of 38:62 (~3:5), which is close to the ratio of the 4Z and 4E isomers in the original dienophile (II) (see [1]). The PMR spectrum of the ester (IV) contains a double set of signals of similar type, the integral intensities of which are in ratio of ~5:3 (Table 3). A similar pattern is observed in the ¹³C NMR spectrum of the ester (IV). Comparison of the data from NMR and GLC shows that the minor isomer has the 1'Z configuration, while the main (and less volatile) isomer has the 1'E configuration (Table 3).

In the binary mixture of diene esters (XIII) + (XIV), obtained during thermolysis of the mixture of cyclic adducts of "citral dieneamine" and methyl acrylate [(XI) + (XII)], the components are in a ratio of 67:33 (in the order of emergence from the column during GLC analysis). In the PMR spectrum of this mixture the singlet of the CH_3 group at the C⁴ atom of the ring is most informative; its integral intensity is ~2H instead of the maximum possible value of 3H. The signals from the Z-directed CH_3 group in the side chain at δ 1.55 and 1.64 ppm have integral intensities in a ratio of 2:1, while the integral intensity of the signals of the allyl (CH_2 and CH) protons at δ 2.0-2.9 ppm corresponds to 6H instead of 5H for (XIII) and 8H for (XIV). This agrees with the ratio of the components determined by GLC. The main (more volatile) isomer thus has the structure (XIII). Analysis of the mixture (XIII) + (XIV) by GLC-MS leads to the same conclusion. The first and second components in order of emergence have different types of fragmentation in the mass spectrum; the main isomer (XIII) is similar in the type of dissociation to the previously studied [8] highest analog (XX), while the minor isomer (XIV) is similar to the highest analog (XXI) (cf. [10]).

Relative intensity of ions, %

						m/z						
Compound	220 (M ⁺)	218	205	189	177	161	152	151	150	137	119	107
(XIII)	10.8	-	-	7.8	-	-	19.0	100	63.0	10.0	73.0	36.0
(XIV)	60.0	9.4	7.8	14.0	6.7	12.2	81.0	36	100	13.3	23.5	15.7

In the ester (XIII) cleavage of the bisallyl bond between the C^5 atom of the ring and the isopentyl side chain is preferred with respect to energy. The molecular ion of the ester (XIII) is, therefore, relatively weak, and the base peak in the spectrum (m/z 151) corresponds to the elimination of the isopentyl radical from the M⁺ ion. Only the less favorable primary allyl cation can form from the molecular ion of the ester (XIV) during cleavage of the bisallyl bond in the side chain, and the intensity of the ion with m/z 151 is therefore lower than in the case of the ester (XIII). Instead of this partial aromatization of the M⁺ ion to the ion with m/z 218 and elimination of the C_5H_8 molecule from both ions, leading to the strongest ions in the spectrum of (XIV) at m/z 152 and 150, are observed. During GLC analysis of the three-component mixture formed in the reaction of the "citral dieneamine" with the monoester (III) three peaks were observed with R_t 7.48, 8.64, and 9.35 min and intensity ratios of ~14:23:63. Comparison of the weight fraction of the components with the integral intensities of signals of the same type in the PMR spectrum of this mixture (Table 3) shows that the main component corresponds to the doublet of the proton at C² with δ 7.00 $(J_{2,3} = 6 \text{ Hz})$, the signal of the proton at C⁶ with 3.56 d.d.d (the M part of an ABMX system with $J_{AM} = 1.8$, $J_{BM} = 8.5$, and $J_{6,1} = 10$ Hz),* the merging signal from the four-spin system of the protons at C⁴a and C⁴b (characteristic for $v_0 \delta \le 5$ Hz) with δ 2.15, and the singlets of the CH₃ groups at C² with δ 1.62 (or 1.65) and 1.70 (or 1.75) ppm; the signal characteristic of the CH_3 group at the C⁴ atom does not belong to this component. Thus, the principal component of the mixture must be assigned the structure (XIV). The signals from the other two components differ in that the signal of the proton at C^6 in the component with R_t 8.64 min looks like the doubled M part of a BM system with $J_{BM} = 5$ and $J_{6,1}$ = 10 Hz, while the analogous signal for the component with R_t 7.48 min (at δ 3.48 ppm) looks like a doublet with $J_{AM} = 0$ and $J_{6,1} = 7$ Hz (which agrees with the diaxial arrangement of the substituents and C⁵ and C⁶). In both compounds there is a CH₃ group at C⁴, the signals from which (δ 1.87 and 1.89) are in a ratio of approximately 14:23. Thus, according to the data from the PMR spectrum, the component with R_t 7.48 min can be assigned a structure with the 5,6-trans configuration trans-(V), while the component with Rt 8.64 min can be assigned a structure with the 5,6-cis configuration cis-(V). Such an assignment is favored by the result from thermolysis of the mixture of amino esters (VIII) + (IX) (see above) and the data from the PMR spectrum of the two-component mixture (V):(VI) = 9:91 with R_t 7.48 and 9.35 min.

The obtained data agree with the data from GLC-MS analysis of the two- and three-component mixture (V) + (VI) [cf. with the GLC-MS data for (XIII, XIV) and also for (XX) and (XXI) [10]].

		1	Relati	ve inte	ensity	of io	ns, %				
						m/z					
Compound	288 (M+)	273	245	243	219	218	215	145	133	119	105
(V)	12	-	-	-	38	29	-	-	67	48	100
(VI)	70	12	18	21	12	7	18	100	12	20	32

In the mass spectrum of the ester (V), as also in the mass spectrum of its analog (XIII), the M⁺ ion is relatively weak, while in the region of large mass numbers the strongest ions correspond to the elimination of the isopentenyl radical (m/z 219) and isopentene (m/z 218). The molecular ion of the ester (VI), like the ion of its analog (XIV), is more stable; the successive elimination of COOEt and C_5H_{10} transforms it into the strong $C_{11}H_{13}$ ⁺ (m/z 145) ion.

EXPERIMENTAL

We used the same spectroscopic and chromatographic technique as in the previous paper [1]. The distribution of the isotopically labeled esters (V)-d and (VI)-d with respect to the mass numbers was calculated by analogy with the method in [11]. Compounds (Ia-c, II, III, VII) were obtained according to [1].

^{*}From the spin-spin coupling constants it follows that the dihedral angles $\varphi_{am} \sim 80^{\circ}$ and $\varphi_{bm} \sim 40^{\circ}$, and this agrees with the equatorial position for $H_{\rm m}$ and the axial position for the substituent at C⁶. The axial position for the substituent at C⁶ is typical of all our obtained derivatives of cyclohexadienecarboxylic acid.

<u>Mixture of the 1'E and 1'Z Isomers of the Ester (IV).</u> A mixture of 0.15 g (1 mmole) of the dieneamine (Ia) and 0.268 g (1 mmole) of monoethyl citrylidenemalonate (II) in 4 ml of benzene was kept at 20°C for 10 min, after which the volatile products were distilled under vacuum. The residue was chromatographed on a column of 5 g of silica gel. The ester (IV) was eluted with benzene in the form of a colorless oil with $nD^{21} = 1.5127$. The yield was 0.18 g (63%). The PMR spectrum is given in Table 3. Mass spectrum: $[M^+] = 288$. IR spectrum (carbon tetrachloride, v, cm⁻¹): 1706, 1644 w, 1585, 1443, 1378, 830. UV spectrum (ethanol): λ 305 nm (ε 10,500). ¹³C NMR spectrum (deuterochloroform, δ , ppm, J, Hz): 14.4 (CH₃CH₂O); 16.35 (2'-CH₃, E isomer); 17.77 (6'-CH₃); 23.63 (2'-CH₃, Z isomer); 24.22 (4-CH₃); 25.73 > 25.81 (C^{7'}, E and Z isomers); 26.61 > 26.95 (C^{4'}); 30.32 < 30.52 (C⁶); 32.2 (C^{3'}, Z isomer); 36.08 > 36.40 (C⁵); 39.83 (C^{3'}, E-isomer); 60.14 (CH₃CH₂O); 118.8 (C³); 124.3 > 124.66 (C^{5'}, E and Z isomers); 124.85 > 125.43 (C^{1'}); 131.26 > 131.52 (C^{6'}); 133.13 (C²); 135.3 > 135.82 (C^{2'}); 142.61 > 142.67 (C⁴); 167.8 (COOEt).

Mixture of Ethyl 4-Methyl-5-(3'-methyl-2'-butenyl)-6-(2'-methyl-1'-propenyl)-1,3-cyclohexadiene-1-carboxylate (V) and 4-(4'-Methyl-3'-pentenyl)-6-(2'-methyl-1'-propenyl)-1,3-cyclohexadiene-1-carboxylate (VI). a. A mixture of 0.2 g (1 mmole) of the citral dieneamine [(Ib):(Ic) = 96:4] and 0.2 g (1 mmole) of monoethyl prenylideneacetate (III) in 4 ml of benzene was kept at 20°C for 1 h, and the volatile products were distilled under vacuum. The residue was chromatographed on a column of 5 g of silica gel. By elution with benzene we obtained a mixture of three isomeric esters with R_t 7.48, 8.64, and 9.35 min in ratios of 14:23:63 in the form of a colorless oil with np^{22} = 1.5195. The yield was 0.16 g (55%). The PMR spectrum is given in Table 3. IR spectrum (carbon tetrachloride, v, cm⁻¹): 1707, 1641 w, 1583, 1445, 1378, 848, and 838 w. UV spectrum (ethanol): λ 310 nm (ε 11,400). Mass spectrum: [M⁺] = 288. The same reaction in boiling benzene (10 min) gave 0.2 g (69%) of a 40:60 mixture of the esters (V) and (VI).

b. A mixture of 0.54 g (2.67 mmoles) of the dieneamine (Ib, c) and 0.6 g (2.67 mmoles) of the diester (VII) was kept at 20°C for 8 days in 2 ml of absolute benzene. The reaction mass was then washed with 10% hydrochloric acid (3 ml) and with water (2 ml). The combined water-acid solution was extracted with ether $(2 \times 2 \text{ ml})$, and its pH was then brought to 7-8 with sodium carbonate solution, and it was extracted with ether $(2 \times 3 \text{ ml})$. The last ether extract was washed with water and dried over sodium sulfate. After distillation of the solvent we obtained 0.65 g (57%) of a mixture of the aminodiesters (VIII) + (IX), which was uniform in TLC, with $np^{24} = 1.4918$ (cf. the aminodiester in [1]). A 0.65-g sample of (VIII) + (IX) was distilled in a restricted-throat flask (130°C, 0.02 mm Hg), and 0.57 g of an oil with $n_D^{22} = 1.5010$ was obtained. According to TLC and PMR, it contained the original diester (VII). In addition to the signals of the protons corresponding to (VII) (the integral increase for the proton amounted to ~0.65 H), the PMR spectrum of this sample contains signals for the protons which can be assigned to the structure (IX) (integral increase for the proton ~0.3-0.35 H) and traces of signals for the protons from (Ib, c). The signals in the PMR spectrum belonging to (IX) (deuterochloroform, δ , ppm): 1.53 s, 1.6 s, and 1.63 d.s (CH₃ of ally1), 3.1 d.d.d (the M part of an ABMX spectrum with $J_{AM} = 12$, $J_{BM} = 5$, and $J_{6,1'} =$ 10 Hz, H-C⁶), 3.85 m (H-C²) 5.01 m (H vinyl, R at C⁴), 5.2 d.m (H-C¹ J_{6,1} = 10 Hz), 5.35 m $(H-C^3)$, the other signals overlap with the signals of the allyl protons (cf. data for the aminodiester described in [1]). A 0.3-g sample of the mixture containing the aminodiester (IX) in addition to (VII) was boiled with 0.04 g (~0.71 mmole) of potassium hydroxide in 0.5 ml of ethanol. After 10 min the reaction mass was evaporated on a rotary evaporator (50°C, 30 mm Hg), 3 ml of water was added, and the mixture was extracted with ether $(2 \times 2 \text{ ml})$. The aqueous layer was acidified to pH 7 with 10% hydrochloric acid and extracted with ether $(2 \times 3 \text{ ml})$. The ether extract was dried with sodium sulfate, and after distillation of the solvent we obtained 0.15 g of the substance in the form of a resin. Yield of (V):(VI) ~ 9:91 (for the GLC-MS data and PMR spectra, see above) after sublimation (180°C, 0.03 mm Hg) and chromatographic purification amounted to 0.04 g (20% in two stages).

<u>Mixture of Methyl 2-Diethylamino-4-methyl-5-(3'-methyl-2'-butenyl)-3-cyclohexenecar-boxylate (XI) and 2-Diethylamino-4-(4'-methyl-3'-pentenyl)-3-cyclohexenecarboxylate (XII).</u> A mixture of the aminoesters with (XI):(XII) ~ 2:1 was obtained from 2.57 g (1.24 mmoles) of the citral dieneamine [(Ib):(Ic) = 95:4] by the method described for (XVI) in [4]. The yield was 2.72 g (75%), $n_D^{21} = 1.4860$, bp 130-133°C (0.08 mm Hg). PMR spectrum (deuterochloroform, δ , ppm): 0.95 m (6H, N-CH₂CH₃), 1.55-1.85 m (~10H, CH₃ of allyl and H-C⁶), 1.9-2.25 m (~3.7 H, CH₂ of allyl and H-C¹), 2.25-2.75 m (~5.3 H, CH₂-N and H-C⁵), 3.4 m + 3.57 m $(H-C^2)$, 3.65 br.s (3H, CH₃O), 5.12 m (1H, CH=C), 5.46 m (H-C³). IR spectrum (carbon tetra-chloride, v, cm⁻¹): 1744, 1670 w, 1550, 1380, 740.

<u>Mixture of Methyl 4-Methyl-5-(3'-methyl-2'-butenyl)-1,3-cyclohexadienecarboxylate (XIII)</u> and 4-(4'-Methyl-3'-pentenyl)-1,3-cyclohexadienecarboxylate (XIV). A 0.59-g sample (2 mmoles) of the mixture of aminoesters (XI) + (XII) was boiled in 2 ml of o-xylene for 32 h, and the volatile products were then distilled under vacuum. The residue was chromatographed on a column of 8 g of silica gel and eluted with hexane with gradual addition of ether to 5 vol. %. The yield with (XIII):(XIV) ~ 2:1 (GLC and GLC-MS) was 0.41 g (93%); nD¹⁸ = 1.5194. The PMR spectrum is given in Table 3. IR spectrum (carbon tetrachloride, v, cm⁻¹): 1708 s, 1644, 1584, 1437, 1380, 838. UV spectrum (ethanol): λ 304 nm (ε 12,000), 242 nm (ε 5600) [from (XVa)]. The (XV) impurity was also detected by GLC-MS and PMR. A mixture of cyclohexadienecarboxylic acid, obtained from (Ib, c) and methyl acrylate in absolute benzene with subsequent deamination in boiling o-xylene (32 h), had the ratio (XI):(XII) = (XIII):(XIV) = 2:1. If the reaction flask is made airtight during the synthesis of (XI) + (XII) (6 days), the ratio is changed to (XI):(XII) = (XIII):(XIV) = 3:1 (PMR and GLC).

<u>Mixture of 3-Diethylamino-5-methyl-6-(3'-methyl-2'-butenyl)-4-cyclohexene-1,2-dicar-boxylic (VIII) and 3-Diethylamino-5-(4'-methyl-3'-pentyl)-4-cyclohexene-1,2-dicarboxylic (IX)</u> <u>Esters.</u> a. A 0.41-g sample (~2 mmoles) of the mixture (Ib, c) in 0.5 ml of benzene was mixed with 0.29 g (~2 mmoles) of dimethyl fumarate in 0.5 ml of THF. After 30 min the solution was separated from the resin, evaporated, and purified by a method similar to that used for the aminodiesters (VIII) + (IX) (see above). The yield was 0.43 g (61%) of the mixture [(XVIIIb) + (XIXb), R = Me], $nD^{25} = 1.4860$, in a ratio of 45:55. PMR spectrum (deuterochloroform, δ , ppm): 0.95 m (6H: N-CH₂CH₃, 1.59 m + 1.68 m (6H, CH₃-C=) 1.74 br.s (1.35 H, CH₃-C=), 1.95-2.2 m (3.1 H, CH₂-C=), 2.2-2.7 m (4H, N-CH₂ + 1.7 H, CH₂ and CH), 2.7-3.2 m (1.85 H, <u>CH</u>-CO₂CH₃), 3.4-3.8 m (1H, N-CH + 6H, CO₂CH₃), 5.05 (1H, <u>HC</u>=C(CH₃)₂), 5.3-5.6 m (1H, HC=). IR spectrum (thin layer, ν , cm⁻¹): 1742, 1670, 1436, 1378, 1198, 1166.

b. A 0.41-g sample (~2 mmoles) of the mixture (Ib, c) in 0.5 ml of benzene was mixed with 0.29 g (~2 mmoles) of dimethyl maleate in 0.5 ml of THF. After 5 days (TLC and UV) we isolated (by analogy with method a) 0.55 g (~78%) of the mixture [(XVIIIb) + (XIXb), R = Me], $n_D^{23} = 1.4854$, in a ratio of ~45:55. The spectral characteristics agree with those of the sample obtained by method a.

c. A 0.41-g sample (~2 mmoles) of (Ib, c) was mixed with 0.34 g (~2 mmoles) of diethyl fumarate in 0.5 ml of benzene. After 3 h (TLC and UV) we isolated (by analogy with method a) 0.69 g (~92%) of the compounds in the ratio (XVIIIb):(XIXb) 45:55 (R = Et), n_D^{25} = 1.4800. Instead of 6 H in the region of 3.6-3.8 ppm the PMR spectrum (deuterochloroform, δ , ppm) contained signals at 1.25 m (6H, $CO_2CH_2CH_3$) and 4.1 m (4H, CO_2CH_2). In other respects the spectrum was identical with that described in method a. IR spectrum (thin layer, ν , cm⁻¹): 1736, 1663, 1446, 1376, 1180.

d. A 0.41-g sample (~2 mmoles) of the freshly distilled mixture (Ib, c) without the citral impurity was mixed with 0.34 g (~2 mmoles) of freshly distilled diethyl fumarate in 0.5 ml of absolute benzene. (The stopper on the flask was sealed with Teflon tape during the reaction.) After 3 h we isolated (by analogy with method a) 0.66 g (~88%) of the products with the ratio (VIIIb):(XIXb) ~ 92:8 (R = Et), $n_D^{22} = 1.4880$. The PMR spectrum (deuterochloroform) differed from that of the sample obtained in method c in the integral intensity of the proton at 1.74 br.s (~2.8H instead of 1.35H), 1.95-3.8 m (~10.2H instead of 11.65H). In other respects the PMR and IR spectra agreed with the data for the sample obtained in method c.

<u>Reaction of the "Citral Dieneamine" (Ib, c) with Citral.</u> In the tube for the PMR spectra we mixed 40 mg (~0.2 mmole) of the mixture with (Ib):(Ic) ~96:4, 15 mg (~0.1 mmole) of citral (E:Z = 70:30 according to GLC analysis and PMR spectra), and 0.5 ml of deuterochloroform. After 3 h the PMR spectrum was recorded. [The chemical shifts agreed with the data described for the mixture (Ib, c) [1] and for the citral isomers [12].] The ratio of the citral isomers changed to E:Z = 55:45 and (Ib):(Ic) = 90:10.

Reaction of Dieneamines (Ib, c) with D_2O . To 0.2 g (1 mmole) of (Ib, c) in 2 ml of THF we added 1 ml (~50 mmoles) of D_2O . The mixture was stirred and left at 20°C for 6 h. By vacuum distillation we isolated 0.1 g of the products in the ratio (Ib)-d:(Ic)-d = 75:25 (PMR); bp 80-82°C (0.2 mm Hg). The data on deuteroexchange of the protons in (Ib) and (Ic) are given in Table 1.

<u>Reaction of Dieneamines (Ib, c).</u> A 0.4-g sample (2 mmoles) of the mixture (Ib, c) was dissolved in 0.72 g (~20.0 mmoles) of CD₃OD and left at 20°C for 6 h. The solvent was then evaporated on a rotary evaporator, a further 0.72 g (~20 mmoles) of CD_3OD was added, and the mixture was left for 12 h. By vacuum distillation we obtained 0.06 g of the products in the ratio (Ib)-d:(Ic)-d = 70:30 (PMR); bp ~82°C (0.2 mm Hg). The data on the deuteroexchange of the protons in (Ib) and (Ic) are given in Table 1.

Mixture of Deuterated Ethyl 4-Methyl-5-(3'-methyl-2'-butenyl)-6-(2'-methyl-1'-propenyl)-1,3-cyclohexadienecarboxylate (V)-d and 4-(4'-Methyl-3'-pentyl)-6-(2'-methyl-1'-propenyl)-1,3-cyclohexadienecarboxylate (VI)-d. a. A 0.4-g sample (2 mmoles) of the monoester (III) was mixed with 0.4 ml (20 mmoles) of D_2O in 2 ml of dry THF. After 6 h the solvent was evaporated on a rotary evaporator (40°C, 30 mm Hg), the aqueous layer was separated, and a further 0.4 ml of D_2O in 2 ml of dry THF was added. The next day the solvent was evaporated on a rotary evaporator, and the aqueous layer was separated and dried twice by azeotropic distillation with 3 ml of absolute benzene. The residue was 0.4 g.

b. A 0.2-g sample (~1 mmole) of the freshly deuterated acid (III)-d was added to a boiling solution of 0.2 g (1 mmole) of (Ib, c) in 4 ml of absolute benzene. After 1 h the reaction mixture was cooled and passed through 5 g of silica gel with benzene as eluant. We obtained 0.15 g (52%) of a ~1:1 mixture of (V)-d and (VI)-d. The characteristic signals in the PMR spectrum and the absorption in the IR and UV regions were similar to the data for (V) + (VI). The data from GLC-MS analysis are given in Table 2.

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