SYNTHESIS OF TRIENIC *w*-DIMETHYLAMINOCARBONYL COMPOUNDS

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In continuation of studying the characteristics of the stereochemistry and properties of unsaturated aminocarbonyl compounds [1-5] we describe in the present paper the synthesis of the previously unknown compounds of type Me₂N(CH=CH₂)₂CH=C(X)COOMe·[X=COCH₃(I), COOCH₃(II), CN(III)]. We established that these compounds can be obtained by the condensation of aminodienes of type Me₂NCH=CHCH=C(X)COOMe(X=COCH₃(IV), COOCH₃(V), CN(VI)) [6, 7] with CH=CMgBr. The reactions of the vinylogs of the N,N-disubstituted formamide and acetamide derivatives with RMgX, which proceed by either the 1,2- or 1,4(1,6)-addition scheme, are described in [8-11]. The use of Iotich reagents as the RMgX is limited to single examples [10-12]. These examples refer mainly to vinylogs with one double band, which lead to the corresponding vinylacetylenic aldehydes and ketones. However, it is indicated in these papers that this route can be used to obtain Et₂N(CH = CH)_nCOCH₃. We checked this postulation and found that the homolog where n = 3 cannot be obtained by this route.

The reaction of (VII) with CH=CMgBr gave a product in 35% yield, which, based on the UV, IR, and NMR spectral data, was apparently a mixture of (VIII) and (IX) in a 1:1 ratio (as the geometric isomers at the γ , δ double bond), which is formed by the addition of CH= CMgBr to (VII) in both the 1,2 and the 1,6 position.

$$(CH_3)_2NCH = CHCH = CHCOCH_3 \xrightarrow{CH \equiv CMgBr} CH \equiv C - CH = CH - CH = CHCOCH_3 \xrightarrow{(IX)} (VII) \xrightarrow{CH \equiv CMgBr} CH \equiv C - CH = CH - CH = CHCOCH_3 \xrightarrow{(IX)} (VIII)$$

We were unable to add Me₂NH to the mixture of (VIII) and (IX), which is in agreement with the data given in [13] regarding the exceedingly slow addition rate of Me₂NH to CH=CCH=CHCHO.

It was shown by us that the presence of two electron-acceptor groups in compounds of the (IV)-(VI) type facilitates their condensation with $CH\equiv CMgX$, and also substantially activates the triple bond in the formed butadienylacetylenic esters (X), (XI), (XII), which makes the nucleophilic addition of Me_2NH to the C=CH bond possible.

Thus, from dienic esters (IV)-(VI) and CH=CMgBr, followed by treatment with Me₂NH, were smoothly obtained trienic esters (I)-(III) (Table 1) in good yields, without isolating the labile intermediate butadienylacetylenic esters (X)-(XIII). The latter can be isolated if the product is not treated with the amine. Acetylenic diester (XI) was obtained in this manner, which, based on the NMR spectral data (Table 2), was a mixture of the cis:trans isomers at the γ , δ double bond in a 1:2 ratio. Me₂NH adds smoothly to diester (XI) to give (II).

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TABLE 1. Yields and Constants of (CH₃)₂N(CH=CH)₂CH=C(X)COOCH₃

Com-	x	Yield,	mp. °C	Empirical	Fou	ınd, %		Calculated, %			
		70		formula	ula C H	н	N	с	н	N	-
(I) (II) (III)	COCH3 COOCH3 CN	$ \begin{array}{r} 68 \\ 62,5 \\ 56 \end{array} $	102-103 82-83 131-134	C12H17NO3 C12H17NO4 C12H14N2O2	$64,57 \\ 60,25 \\ 64,00$	7,67 7,20 6,80	$6,54 \\ 5,89 \\ 13,66$	$64,55 \\ 60,24 \\ 64,06$	$7,68 \\ 7,16 \\ 6,84$	6,27 5,85 13,58	-

*After recrystallization from abs. MeOH.

ζεδ γβ α

TABLE 2. NMR Spectrum of CH=CCH=CHCH=C(COOCH₃)₂ [(XI) (in CD₃OD)]

	Chemical s	hifts δ,	^{<i>J</i>} , Hz						
Isomer*	CH30C0	β	Ŷ	δ	Q. Q.	β, γ	γ, δ	δ, ζ	γ,ζ
trans- cis	3,72; 3,73; 3,76†	7,35 7,8	6,94 6,84	6,15 5,94	3,8 3,98	11,2 12	14 10	$\overset{2,3}{3}$	0,8

*cis/trans Ratio = 1/2.

+The isomers were not assigned signals.

We were also interested in whether the above-indicated reactions could be repeated with trienic esters (I)-(III) in order to obtain ω -dimethylaminocarbonyl compounds with four double bonds. The condensation of (II) with CHECMgBr led to the isolation of acetylenic diester (XIII) in 36% yield, but we were unable to add Me₂NH to it.

(II) $\xrightarrow{\text{CH}\equiv\text{CMgBr}}$ CH \equiv C $-(\text{CH}=\text{CH})_2$ CH=C(COOCH₃)₂ (XIII)

The stereochemistry of the synthesized trienic ω -dimethylaminocarbonyl compounds was studied via the NMR spectra, which were obtained on an HR-220 instrument at an operating frequency of 220 MHz. The data for compounds (I) and (II) are given in Table 3. The signals of two stereoisomers are observed in the spectrum of (I), which we assigned to the geometric isomers at the α , β double bond on the basis that the $J_{\beta\gamma}$, $J_{\gamma\delta}$, $J_{\delta\varepsilon}$, and $J_{\varepsilon\zeta}$ are the same in both isomers and, in addition, that the stereoisomers are absent in the case of the same substituents at C_{α} in compound (II). The value $J_{\epsilon\zeta} = 12.8$ Hz and its comparison with the value of the spin-spin coupling constant [SSCC] of the protons at the double bond in the trans- and cis-enaminoketones (respectively, 12-15 and 6-8 Hz [14]) make it possible to conclude that (I) and (II) have the transconfiguration of the protons at the ε , ζ bond. The greatest change in the chemical shift when going from one geometric isomer at the α , β double bond to the other isomer is experienced by the H_v proton when compared with the other methine protons. The Stuart-Briegleb models show that only with an S-trans arrangement of the α , β and γ , δ double bonds do substitutents at C_{α} exert a greater steric effect on H_Y. Taking this into account, and also taking into consideration the value $J_{\beta\gamma}$ = 12.8 Hz, it was concluded that (I) and (II) exist predominantly as the S-trans conformers at the β , γ bond. The value $J_{\gamma,\delta} = 14$ Hz makes it possible to assign the studied compounds to the trans isomers at the γ, δ bond. The relatively small difference between $J_{\delta,\epsilon} = 11.2$ and $J_{\beta,\gamma} = 12.8$ Hz makes it possible to assume that (I) and (II) have an S-trans arrangement of the γ , δ - and ε , ζ double bonds.

When the temperature dependence of the NMR spectra was studied it was found that in (I) and (II) the rotation around the $C_{\alpha} = C_{\beta}$ bond is relative easy, while that around the C-N bond is hindered. Similar effects were described by us previously [1, 2] for the corresponding dienes.

The UV spectra of (I)-(III) are summarized in Table 4, where for comparison we have given the UV spectra of the analogous compounds with one and two double bonds (n = 0, 1) [2, 15], and also the UV spectra of some ω -aminocarbonyl compounds (n = 0, 1, 2, 3), but with one electron-acceptor group (X¹ = H).

As was already mentioned [13, 16-18], in the compounds $(X^1 = H)$ (see Table 4) the bathochromic shift of λ_{max} decreases noticeably for each subsequent member of the series

αβγ

			Chemical shifts δ, ppm									J	, Н г	
Com - pound	х	Isomer	MeCO	MeO ₂ C	NMe ₂	β	Y	δ	ε	ζ	β, γ	γ, δ	δ,ε	ε, ζ
(I) (II)	MeCO MeO₂C	cis* trans	$^{2,41}_{2,35}$	$3,75 \\ 3,82 \\ 3,75$	2,84 2,84 2,91	$7,52 \\ 7,58 \\ 7,57 \\ 7,57 \\ $	$7,02 \\ 6,57 \\ 6,57 \\ 6,57$	$6,90 \\ 6,94 \\ 6,82$	$5,30 \\ 5,30 \\ 5,25$	$6,75 \\ 6,75 \\ 6,68$	12,8 12,8 12,8 12,8	14 14 14	$ \begin{array}{r} 11,2 \\ 11,2 \\ 11,2 \\ 11,2 \\ \end{array} $	12,8 12,8 12,8 12,8
				3,82			, i							l i

*Has a cis arrangement of CO_2 Me and H_β, and the cis/trans ratio = 1/2.

TABLE 4. Ultraviolet Spectra* of $(CH_3)_2N(CH=CH)_nCH=C(X^1)X^2$ (in C₂H₅OH)

n	1	H=H		X1=COOCH3								
	X1=CHO		X2=COCH3		X2=COOCH3		X2=COOCH3		X ² =COCH ₃		X2==CN	
	۸†.nm	٤	ኦ, nm	U)	λ, nm	ε	[,] пт	8	λ, _{nm}	ε	λ, n m	٤
0 1 2 3	$283 \\ 361,5 \\ 421,5 \\ 462,5$	37 000 51 000 56 000 65 000	304 380	22 400 48 800	279 350 380	19 200 42 900	288 374 460	19 600 54 400 57 600	312 400 499	15 616 57 000 91 000	310 386 482	21 000 60 000 87 000

*The principal maxima are given. †In CHCl₃.

with increase in n. The difference between the λ_{max} ($\Delta\lambda_{max}$) of the compounds with n = 1 and 0 is 78 nm (X¹ = H, X² = CHO) and 71 nm (X¹ = H, X² = COOCH₃); the $\Delta\lambda_{max}$ when going from compounds with n = 1 to 2 is, respectively, 60 and 30 nm; from n = 2 to 3 the $\Delta\lambda_{max}$ is now 40 nm (X¹ = H, X² = CHO). These data are in agreement with the character of the changes in the dipole moments and testify to the fact that the degree of mesomeric charge transfer from the unshared electron pair of nitrogen to the oxygen atom decreases with increase in n, i.e., the interaction between the terminal substituents weakens with elongation of the polyene chain [13, 16, 17, 19].

However, this phenomenon is not observed in compounds (I), (II), and (III), (X¹ = COOCH₃), which have two electron-acceptor substituents. In this case the bathochromic shift of λ_{max} when going from n = 1 to 2 ($\Delta\lambda_{max}$ 86 nm, X² = COOCH₃; $\Delta\lambda_{max}$ 99 nm, X² = COCH₃; $\Delta\lambda_{max}$ 96 nm, X² = CN) is not only not smaller, but even somewhat greater than when going from n = 0, to 1 ($\Delta\lambda_{max}$ = 86 nm, X² = COOCH₃; $\Delta\lambda_{max}$ 88 nm, X² = COCH₃; $\Delta\lambda_{max}$ 76 nm, X² = CN).

EXPERIMENTAL METHOD

The NMR spectra of compounds (VIII), (IX), and (XI) were taken on a DA-60-IL instrument using HMDS as the internal standard.

Reaction of 6-Dimethylamino-3,5-hexadien-2-one (VII) with CH=CMgBr. With stirring, to a solution of 2 g of ketone (VII) in 30 ml of abs. THF at 20° was added a solution of CH=CMgBr, which was prepared from 1 g of Mg in 70 ml of abs. THF. The reaction mass was heated at 40° for 40 min, cooled, treated with 4 N H₂SO₄ solution, and extracted with ether. The extract was washed with water, dried over MgSO₄, evaporated, and the residue was vacuum distilled. We obtained 0.6 g (35%) of a mixture of (VIII) and (IX), bp 120-125° (0.3 mm), $n_D^{2°}$ 1,5570. NMR spectrum (CD₃OD, δ , ppm): (VIII) 1.97 and 1.84 n. s. (CH₃C=); 3.98 and 3.57 s (CH=); 9.5 d (CHO); J_{CHO,H\alpha} = 8 Hz; (IX) 2.2 and 2.4 s (CH₃CO); 3.64 d (CH=), J_{CH=}, H δ = 3 Hz and 3.85 g (CH=), J_{CH=,H} δ = 3, J_{CH=H γ} = 1 Hz.

The signals of the methine protons are found in the 5.6-7.8 ppm region, which were not assigned due to the complexity of the spectrum.

Ultraviolet spectrum of (VIII) and (IX) (in EtOH): $\lambda_{max} 296 \text{ nm}$ ($\epsilon 30500$) (C=C-C=CH=CHC) [13].

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Infrared spectrum of (VIII) and (IX) (ν , cm⁻¹): 3310 and 2140 (CH=C), 1690 and a shoulder at 1680 (CHO and CH₃CO), 2370 (CHO), 1590 and 1615 (C=C).

<u>Methyl Ester of 7-Dimethylamino-2-acetyl-2,4,6-heptatrienoic Acid (I)</u>. To the CH=CMgBr, obtained from 1.92 g (0.08 mole) of Mg in 150 ml of abs. THF, was added at 0°, in 30 min, 8.4 g (0.042 mole) of (IV) in an acetylene stream.* The reaction mass was stirred at 20° for 1 h and at 50-60° for 15 min, after which it was cooled to 0°, treated with saturated NH₄Cl solution, extracted with ether, and then with CHCl₃. To the combined extract⁺ was added an alcohol solution of Me₂NH. After drying over MgSO₄ and evaporation we obtained 6.5 g of (I) as brownish-red crystals with mp 102-103° (from abs. MeOH).

Methyl Ester of 7-Dimethylamino-2-carbomethoxy-2,4,6-heptatrienoic Acid (II). Diester (II) was obtained from diester (V) in the same manner as (I).

Methyl Ester of 7-Dimethylamino-2-cyano-2,4,6-heptatrienoic Acid (III). Ester (III) was obtained from cyanoester (VI) in the same manner as (I). After adding (VI), the reaction mass was stirred at ~20° for 1 h and at 30° for 15 min.

Methyl Ester of 2-Carbomethoxy-2,4-heptadien-6-ynoic Acid (XI). To the CHECMgBr (from 0.96 g of Mg in 100 ml of abs. THF) at 0° was added 3.5 g of (V), the mixture was stirred at ~20° for 20 min and at 60° for 15 min, after which it was cooled, treated with 4 N H₂SO₄ solution, and extracted with ether. The extract was washed with water, dried over MgSO₄, and evaporated. The residue (2.5 g, λ_{max} (in C₂H₅OH), 290 nm, ε 22,400) was subjected to preparative TLC on SiO₂ in the system: 1:2 acetone-hexane. We isolated (XI) as a yellow oil; nD²⁰1.5490; max (in C₂H₅OH) 290 nm (ε 44,800). Infrared spectrum (ν , cm⁻¹); 3310 and 2110 (HC \equiv C), 1720 (COOCH₃). Compound (XI) decomposes when vacuum distilled at 0.1 mm. The treatment of (XI) with methanolic Me₂NH solution gave diester (II), which was identical with that described above.

Methyl Ester of 2-Carbomethoxy-2,4,6-nonatrien-8-ynoic Acid (XIII). To a stirred solution of 3 g of diester (II) in 30 ml of abs. THF at ~20° was added a solution of CH=CMgBr, obtained from 0.72 g of Mg in 70 ml of abs. THF. The reaction mixture was heated at 40-45° for 30 min. The end of reaction was checked by the disappearance in a sample, treated with saturated NH₄Cl solution, of λ_{max} 460 nm, which belongs to the starting diester (II). After cooling, the mixture was treated with 4 N H₂SO₄ solution, and extracted with ether; and the ether extract was washed with water, dried over MgSO₄, and evaporated below 35°. We obtained 1 g (36.5%) of diester (XIII) with mp 78-80° (decompn.) (from abs. MeOH). λ_{max}

(in C₂H₅OH) 330 nm (ε 34,285). IR spectrum (XIII) (ν, cm⁻¹): 2100, 3275 (CHΞC), 1715 (COOCH₃). Found: C 64.94; H 5.81%. C₁₂H₁₂O₄. Calculated: C 65.44; H 5.49%.

The compound turned to a tar when a solution of diester (XIII) in MeOH was treated with methanolic Me_2NH solution.

CONCLUSIONS

1. A study was made of the reaction of some unsaturated aminocarbonyl compounds with the lotsich reagent.

2. Some trienic ω -dimethylaminocarbonyl compounds were synthesized and their configuration was established by the NMR method.

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*The yield of (I) drops when the reactants are added in reverse. +The UV spectrum of the extract has λ_{\max} 294 nm (X) and 499 nm (I) of equal intensity, which testifies to the partial addition of Me₂NH to the CECH bond.

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