sym-TRIAZINE DERIVATIVES.

8*. STRUCTURE AND FURTHER REACTIONS OF PRODUCTS FORMED IN THE REACTION OF 2,4,6-TRIETHOXYCARBONYL-sym-TRIAZINE WITH ARYLHYDRAZINES

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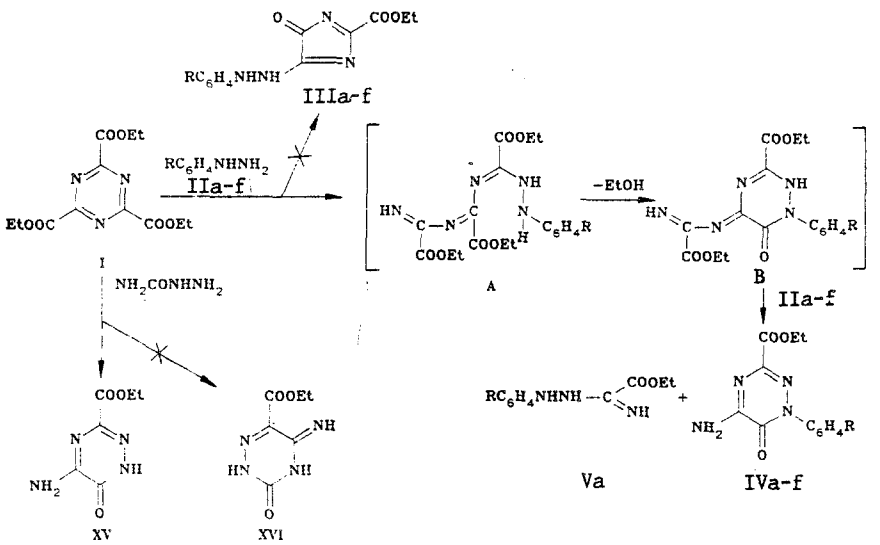
It has been demonstrated, based on detailed spectral analysis and chemical reaction studies, that the products of the reactions of arylhydrazines or semicarbazide with 2,4,6-triethoxycarbonyl-sym-triazine are 1,2,4-triazine derivatives.

We have previously established that reaction of 2,4,6-triethoxycarbonyl-sym-triazine (I) with phenylhydrazine (IIa) proceeds via recyclization [2], which is general in nature for arylhydrazines IIa-f, independent of substituents present in the phenyl ring [3]. The structures proposed for the recyclization products were 2-ethoxycarbonyl-4-arylhydrazino-5-oxoimidazoles IIIa-f [2, 3].

In the present paper we have concluded, based on detailed spectral analysis, that structure III does not in fact correspond to the structure of the recyclization products, and have deduced that the products represent instead 5-amino-1-aryl-6-oxo-3-ethoxycarbonyl-1,6-dihydro-1,2,4-triazine derivatives (IVa-f). We have also studied the chemical properties and structures of the further reaction products of one of the members of this class of compounds, namely IVa, and have refined the structure of a 1,2,4-triazine derivative prepared previously by us [4].

Scheme 1



II—V a R=H; II—IV b R=2-CH_3, c R=3-CH_3, d R=4-CH_3, e R=4-Cl, f R=4-NO_2

*Communication 7, see [1].

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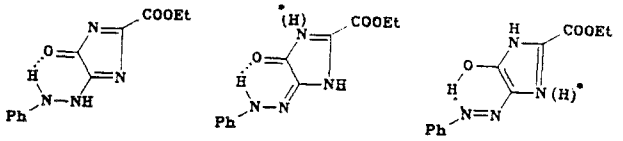
TABLE 1. ^{13}C-NMR Spectra of 1,2,4-Triazines IVa, VIIa-IXa, XIIa, and XV

Compound	δ, ppm (J, Hz) in DMSO-D_6									
	1-Ph				$C_{(3)}$	3R			$C_{(5)}$	$C_{(6)}$
	$C_{(1')}$	$C_{(2')}$	$C_{(3')}$	$C_{(4')}$		CO	CH_2	CH_3		
IVa	140,2 ($^3J_{CH}$=8,5, t; $^2J_{CH}$=2,5, t)	125,2 ($^1J_{CH}$=165,5,d; $^3J_{CH}$=6,0, t)	128,6 ($^1J_{CH}$=161,5, d; $^3J_{CH}$=8,0,d)	128,3 ($^1J_{CH}$=161,5,d; $^3J_{CH}$=7,0, t)	141,8	162,0 ($^3J_{CH}$=3,2, t)	61,3 ($^1J_{CH}$=148,4; t; $^2J_{CH}$=4,5, q)	14,0 ($^1J_{CH}$=127,0, q; $^2J_{CH}$=2,7, q)	157,6*	149,6 ($^3J_{CH}$ = 8,5, d; 2,5, d)
VII[a]	140,1 ($^3J_{HC}$=7,0,t)	125,1 ($^1J_{CH}$=165,5, d)	128,5 ($^1J_{CH}$=162,0, d,	128,0 ($^1J_{CH}$=162,0,d)	132,8	159,9	—	—	154,6**	154,3**
VIII[a]	140,4 ($^3J_{CH}$=8,5, t; $^2J_{HC}$=2,0, t)	124,8 ($^1J_{CH}$=165,0, d; $^3J_{CH}$=6,0, t)	128,4 ($^1J_{CH}$=162,0, d, $^3J_{CH}$=7,5, d)	127,5 ($^1J_{CH}$=161,5,d, $^3J_{HC}$=7,5, t)	132,8 ($^1J_{CH}$= =210,0, d)				155,2 ($^3J_{CH}$=7,0,d)	154,7
IXa	140,1 ($^3J_{CH}$=6,5, t)	125,2 ($^1J_{CH}$=164,5)	128,6 ($^1J_{CH}$=162,5)	128,1	132,0	158,5 ($^3J_{CH}$=3,2, t)	62,6 ($^1J_{CH}$=149,5; $^2J_{CH}$=4,5, q) 63,4	13,8 ($^1J_{CH}$=127,3; $^2J_{CH}$=2,7) 13,9	154,6**	154,1**
XIIa***	139,3 ($^3J_{CH}$=8,0, t; $^2J_{CH}$=2,0, t)	124,2 ($^1J_{CH}$=166,0, d)	128,7 ($^1J_{CH}$=162,0,d)	128,2 ($^1J_{CH}$=161,5,d)	134,9 ($^3J_{CH}$= =2,7, q)	158,8 ($^3J_{CH}$=3,5, t)	($^1J_{CH}$=149,0, t; $^2J_{CH}$=4,4, q)	($^1J_{CH}$=127,5,q ; $^2J_{CH}$=3,0, t)	155,1 ($^3J_{CH}$=2,7,q)	151,9
XV					142,2	162,0 ($^3J_{CH}$=3,1, t)	61,0 ($^1J_{CH}$=148,3, t; $^2J_{CH}$=4,5,q)	14,0 ($^1J_{CH}$=127,0,q , $^2J_{CH}$=2,6, t)	157,2	150,8 ($^3J_{CH}$=8,2,d ; 3,0,d)

*Isotopic shift upon deuteration, 0.06 ppm.
**The reverse signal assignment is also possible.
***The spectrum was taken in $CDCl_3$ solution.

Analysis of the NMR and mass spectra of the reaction product of phenylhydrazine IIa with triazine I revealed a series of spectral parameters which were inconsistent with the proposed structure IIIa. For instance, in the ^{13}C-NMR spectrum (Table 1), the chemical shift (CS) values of the phenyl ring carbon atoms in the recyclization product did not correspond to the expected values for one of the potential tautomeric forms of imidazolone IIIa, which differ from one another in the structure of the phenylhydrazine residue:



*We have shown in parentheses the alternative proton position for the tautomeric form with the identical phenylhydrazine residue structure.

The structural inconsistency is indicated first of all by the substantial discrepancy (> 12 ppm) between the CS of the $C_{(1)'}$ and $C_{(2)'}$ carbon atoms in the phenyl substituent in the recyclization product and the analogous CS values in model compounds (Table 2, compounds 2-4) containing a phenylhydrazine residue with the same structure as in the possible tautomeric forms of imidazolone IIIa. The CS value of the $C_{(1)'}$ atom in the recyclization product was found to be significantly lower than in each of the model compounds, but was very similar in magnitude to the signal for the $C_{(1)'}$ atom in N-arylamides (Table 2, compound 5). Further argument against structure IIIa is provided by the absence of evidence of intramolecular hydrogen bond (IMHB) formation in the PMR spectrum (Table 3) of the recyclization product, despite the feasibility of chelate-type hydrogen bond formation from any of the possible tautomeric forms of imidazolone IIIa. The absence of IMHB in the recyclization product is suggested on the basis of the similar upfield signal position for the two active (mobile) hydrogen atoms (at $\delta \approx 7$ ppm in $CDCl_3$), which are shifted 1.5 ppm downfield in DMSO-D_6, apparently due to intermolecular hydrogen bond formation with the solvent (Table 3). Similar inconsistencies are not observed for the recyclization product structure IVa; all of the spectral data obtained for this compound are consistent with this structure. Thus, for example, in the ^{13}C-NMR spectrum of compound IVa, in addition to the low value of $\delta_{C_{(1)'}}$, mentioned above, indicative of the presence of a $-C_{(6)}(O)-N_1-Ph$ functional group, we note also the vicinal coupling between the $C_{(6)}$ atom and the two amino group protons attached to $C_{(5)}$ ($^3J_{C_{(6)}NH_A} = 2.5$; $^3J_{C(3)NH_B} = 8.5$ Hz); these two protons are nonequivalent due to restricted rotation about the $C_{(5)}$-N bond. The presence of an isotopic shift for $C_{(5)}$ in addition to to the $^3J_{CH}$ values given in Table 1 have allowed us to assign all of the signals in the ^{13}C-NMR spectrum of the recyclization product based on structure IVa.

Analysis of the mass spectra of compound IVa and its analogs IVc, IVe, and IVf reveals that the principal peaks belong to the $[M - COOEt]^+$ and $\Phi_1-\Phi_3$ ions (Table 4). The m/e values for the ions Φ_1 and Φ_2 depend on the substituent in the benzene ring, which provides unequivocal evidence for the inclusion of the aryl group in the composition of these ions. The ion Φ_3, on the other hand, has the same m/e value in the spectra of all of the compounds IVa-f. Deuteration of samples of IVa and IVe using CD_3OD in a system with direct injection into the mass spectrometer† showed that the Φ_2 ion does not contain any active hydrogen atoms, while the ions Φ_1, Φ_3, and Φ_4 contain two active (exchangeable) protons. For the Φ_1 ion the ratio of intensities of the deuterium-containing fragments versus the intensity of the non-deuterium-containing ion $I_{\Phi_1+1}/I\Phi_1$ and I_{Φ_1+2}/I_{Φ_1} was found to be about two times lower than for the analogous ratios in the molecular ion group. This suggests that the ion Φ_1 is a two-component ion. Investigation of the high-resolution mass spectrum of compound IVa revealed that the 119†† peak is composed of two ions Φ_1' and Φ_1'' (Table 4. The formation of an ion of composition C_7H_5NO is difficult to formulate based on structure IIIa, but is in excellent accord

†Based on its mass spectral data, taking into account a monoisotopic contribution, the exchange product contained 25% di-, 45% mono-, and 30% nondeuterated derivatives of IVa.
††Both in the text and in Scheme 2 the numbers which are given to characterize the ions are their m/e values.

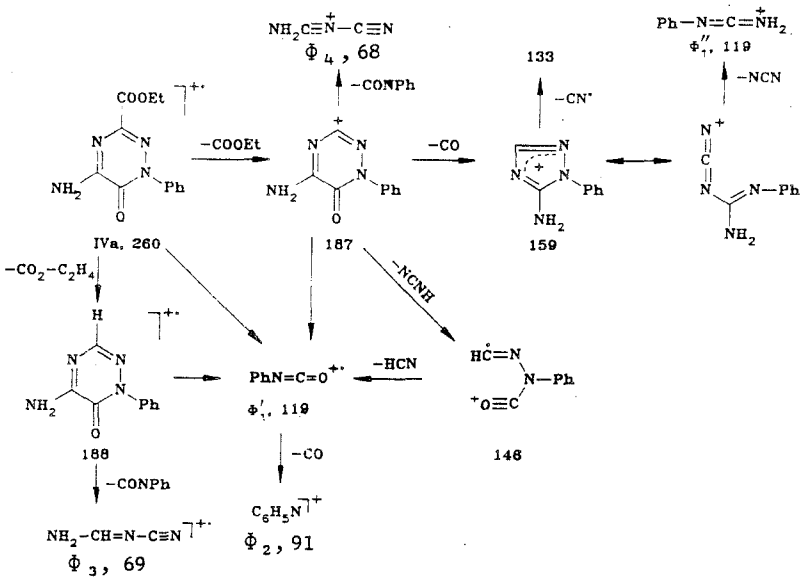
TABLE 2. Chemical Shift Values for the Phenyl Substituent Carbon Atoms ($C_{(1')}$-$C_{(4')}$) in the Recyclization Product Triazine IVa and in Various Model Compounds

No.	Compound	Chemical shift, ppm			
		$C_{(1')}$	$C_{(2')}$	$C_{(3')}$	$C_{(4')}$
1	IVa	140,2	125,2	128,6	128,2
2	PhNHNHPh	148,7	112,2	129,2	119,7
3	PhN=NPh	152,5	122,8	129,0	130,9
4	$PhNHN=CHC_6H_4-NO_2$ (4)	143,5	113,0	129,4	121,2
5	$PhNHCOCH_3$ [5. — P. 47]	139,5	118,5	128,5	122,5

with structure IVa, containing on O=CNPh functional group arrangement. According to their DADI spectral data the ions Φ_1 and Φ_2 are formed via extensive fragmentation of the [M − COOEt]+ ion. The overall sequence of decomposition or decay of compound IVa and its analogs is entirely consistent with the proposed structure and can be described by the paths shown in Scheme 2.

Based on the structures of the recyclization products IVa-f we propose the following scheme for the conversion reactions of triazine I upon treatment with arylhydrazines IIa-f. One molecule of arylhydrazine IIa-f apparently adds to the C=N bond in triazine I, and is subsequently cleaved (Scheme 1). The resulting product A cyclizes to give a 1,2,4-triazino compound B via C—N bond closure between the β-N atom in the arylhydrazine moiety of IIa-f and the carbonyl C atom in an ester group, accompanied by dissociation of a molecule of ethanol. Derivative B, upon attack by a second arylhydrazine molecule, undergoes cleavage of the C—N bond in the amidine fragment, resulting in the formation of 1-aryl-3-ethoxycarbonylamidrazone (V) and 5-amino-1-aryl-6-oxo-3-ethoxycarbonyl-1,6-dihydro-1,2,4-triazine (IV). This hypothetical scheme has been verified by the isolation of 1-phenyl-3-ethoxycarbonylamidrazone (Va) in 49% yield from the reaction mixture, and by the virtual absence of starting material I among the reaction products at a I to IIa reagent ratio equal to 1:2.5.

Scheme 2



The chemical properties of compound IVa are consistent with the structure of a 1,2,4-triazino derivative.

In an aqueous alcohol solution of alkali the ester functional group in compound IVa is saponified to give acid VIa; the PMR spectrum of the latter does not contain any carboethoxy group proton signals, but does exhibit a broad signal for the COOH group proton at $\delta \approx 13$ ppm, while the CS values of the re-

TABLE 3. Chemical Shift Values in the PMR Spectra of 1,2,4-Triazines IVa, VIa-XIIIa, XV

Compound	Solvent	Hydrogen atom or substituent in position							
		1			3			4	5
		C'2H(Ph), m	C'3H(Ph), m	C'4H(Ph), m	CH_2q	CH_3	other		
IVa	DMSO-D_6	7,63	7,53	7,44	4,27	1,27t		—	8,25 br.; 8,68 br. (NH_AH_B)
IVa	$CDCl_3$	7,73	7,51	7,45	4,45	1,42 t	13,0br. (COOH)	—	6,90 br.; 7,02 br. (NH_AH_B)
VIa	DMSO-D_6	7,64	7,52	7,44			—	—	8,20 br.; 8,60 br. (NH_AH_B)
VIIa	DMSO-D_6	7,53	7,50	7,44		—*		—*	—
VIIIa	DMSO-D_6	7,56	7,48	7,41			7,73 s	12,4 br.	—
VIIIa	$CDCl_3$	7,64	7,45	7,39			7,57 s	—	—
IXa	$CDCl_3$	7,63	7,50	7,43	4,49	1,43 t		10,0 br.	—
Xa	$CDCl_3$	7,71	7,51	7,44		3,97 s			7,0 br.; 8,05 br. (NH_AH_B)
XIa	$CDCl_3$	7,70	7,50	7,41		3,97 s			7,05br. (NH); 3,32 d (CH_3)**
XIIa	$CDCl_3$	7,65	7,49	7,40	4,46	1,49 t		3,63 s (CH_3)	—
XIIIa	$CDCl_3$	7,72	7,49	7,41	4,44	1,42 t			7,03 br. (NH); 3,23 d (CH_3)**
XV	DMSO-D_6	12,9 (N_1H)			4,24	1,27 t			7,91br.; 8,38 br. (NH_AH_B)
XV	DMSO-D_6–$CDCl_3$ 1 : 10	12,4 (N_1H)			4,40	1,39 t			6,86 br.; 7,01 br. (NH_AH_B)

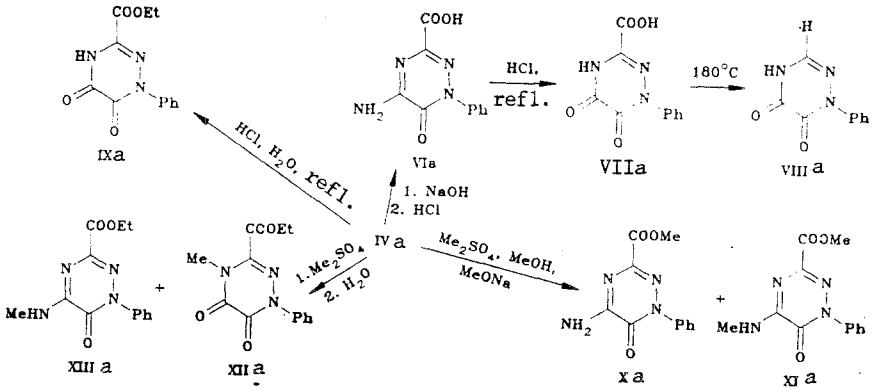
*General broad signal at $\delta \sim 12.6$ ppm.
**$J_{NHCH_3} \approx 5.3$ Hz.

TABLE 4. Characteristic Ions in the Mass Spectra of Compounds IVa-XIIIa, XV

Compound	m/e (I_{rel}, %)									
	M·	[M–HCOOR]·	[M–COOR]·	[M–COOR, –CO]·	[M–CO]·	[M–2CO]·	Φ_1	Φ_2	Φ_3	Φ_4
IVa	260(100)	188(10)	187(30)	156(16)	—	—	119(21)*	91(44)	69(27)	68(12)
IVc	274(100)	202(18)	201(57)	173(67)	—	—	133(39)	105(51)	69(75)	68(19)
IVd**	294(100)	222(13)	221(30)	193(11)	—	—	153(32)	125(93)	69(82)	68(18)
IV	305(100)	233(46)	232(47)	204(5)	—	—	164(23)	136(23)	69(67)	68(11)
VIa	232(100)	188(<5)	187(10)	159(10)	—	—	119(7)	91(71)	69(21)	68(7)
VIIa	233(28)	—	—	—	205(8)	—	119(8)	91(100)	—	—
VIIIa	189(56)	—	—	—	161(17)	—	—	91(100)	—	—
IXa	261(50)	—	—	—	233(24)	205(15)	119(11)	91(100)	—	—
Xa	246(92)	188(6)	187(13)	159(13)	—	—	119(17)	91(100)	69(14)	68(10)
XIa	260(100)	202(5)	201(12)	173(6)	—	—	119(6)	91(69)	83(12)	82(10)
XIIa	275(23)	—	—	—	271(11)	219(12)	119(45)	91(100)	—	—
XIIIa	274(100)	202(15)	201(45)	173(12)	—	—	119(16)	91(60)	83(39)	82(19)
XV	184(54)	112(100)	111(21)	83(9)	—	—	—	—	69(97)	68(18)

*Φ_1' ion. Measured: 119.0371. C_7H_5NO. Calculated: 119.0379 (54%). Ion Φ_1''. Measured: 119.0608. $C_7H_7N_2$. Calculated: 119.0609 (46%).
**The mass numbers and intensities are given for the ^{35}Cl-containing ions.

Scheme 3



maining proton signals are analogous to those measured for the precursor ester IVa. The mass spectrum of compound VIa contains an intense peak for M^+ at 232; the electron impact-induced fragmentation of this peak occurs via elimination of a carboxyl group. Further fragmentation of the $[M - COOH]^+$ ion occurs via Scheme 2.

Refluxing compound VIa in dilute hydrochloric acid results in hydrolysis of the amino group and formation of the 5,6-dioxoacid VIIa, which undergoes facile decarboxylation to form 5,6-dioxo-1-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine VIIIa (93% yield). Hydrolysis of the amino group in the recyclization product prior to ester saponification can be achieved via refluxing compound IVa in a dilute aqueous alcohol solution of hydrochloric acid. The yield of the resulting 5,6-dioxo-1-phenyl-3-ethoxycarbonyl-1,4,5,6-tetrahydro-1,2,4-triazine product (IXa) is 85%.

In contrast to the PMR spectra of the amino derivatives IVa and VIa, the PMR spectra of the dioxo compounds VIIa-IXa do not contain signals for the two amino group protons, at $\delta \sim 8.2$ and 8.6 ppm (in DMSO-D_6). At the same time, the multiplicity of the $C_{(6)}$ signal in the non-proton decoupled ^{13}C-NMR spectrum also changes: rather than a quartet as in the spectrum of the amino derivative IVa, a singlet is observed in the spectra of the dioxo compounds VII-IXa.* In addition, the signals for the $C_{(3)}$ atom in the ^{13}C-NMR spectra of these compounds are shifted upfield by about 10 ppm relative to the corresponding signal in the spectrum of the amino derivative IVa, apparently due to enhanced electron donating characteristics of the nitrogen atom in the NH group in the 2- or 4-position of the dioxo derivatives VIIa-IXa, compared to the two "pyridine" type nitrogen atoms in these positions in compound IVa.

Noteworthy in the ^{13}C-NMR spectrum of compound VIIIa is the large value of the direct coupling constant $^1J_{C_{(3)}H} = 210$ Hz, which is characteristic of a CH group located between two nitrogen atoms in azines and azoles [6]. Indirect coupling with the C(3)H proton is traced to the signal at δ 155.2 ppm, which is assigned on this basis to the $C_{(5)}$ atom ($^3J_{C_{(3)}H,C_{(5)}} \approx 7$ Hz). The chemical shift values for the phenyl substituent carbon nuclei are very similar in compounds IVa, and VIa-IXa, which is consistent with the conclusion that the 1,2,4-triazine structure is retained during these indicated transformation reactions.

In the mass spectra of compounds VIIa-IXA, in contrast to IVa and VIa, the M^+ ion peaks have uneven (odd) mass numbers (233 for VIIa, 189 for VIIIa, 261 for IXa); this is indicative, of course, of an odd number of nitrogen atoms in these molecules. The presence of a 5,6-diketo functional group arrangement in the triazine ring leads to a substantial change in the nature of the decomposition pathway for compounds VIIa-IXa compared to IVa (Table 4). Thus, in the spectrum of the dioxo derivative IXa elimination of a COOEt group from M^+ is not observed. Fragmentation or decay instead occurs via cleavage of bonds within the ring to give $[M - CO]^+$ and $[M - 2CO]^+$ ions; elimination of a COOEt group is observed only from these ions, but the intensities of the resulting ions are less than 10 and 6%, respectively. The peak with the maximum intensity in the mass spectra of compounds VIIa-IXa corresponds to the Φ_2 ion, while

*The NH group proton is "acidic," i.e., undergoes facile intramolecular (between the 2-NH and 4-NH tautomers) and intermolecular exchange; this leads to the absence of any kind of interaction (coupling) between this proton and other nuclei in the dioxo derivatives VIIa-IXa.

peaks due to the Φ_3 and Φ_4 ions are missing. Due to the ease of thermal decarboxylation of compound VIIa, its mass spectrum exhibits intense peaks due to $[M - CO_2]^+$ (189) and other ions arising from its decay, such as cleavage of ring bonds and ensuing elimination of CO (161) and C_2O_2NH (118). As the sample injection temperature is increased the intensities of these ions increase significantly. The differences in the decay or fragmentation patterns of the acid and its ester IXa can apparently be explained in terms of the ease of decarboxylation of the acid VIIa.

It should also be noted that the very act of hydrolysis of the amino group in the recyclization product (with concomitant retention of the heterocyclic residue) disproves the previously proposed imidazolone structure IIIa for this material.

Attempted methylation of ester IVa with dimethyl sulfate in methanol solution in the presence of sodium methoxide led primarily to transesterification, namely the formation of methyl ester Xa, whose PMR spectrum is completely analogous to that of ester IVa, except that it contains the appropriate methoxycarbonyl group signals. The molecular weight of ester Xa (246) is 14 amu lower than that of compound IVa, and it eliminates the methoxycarbonyl group in the first stage of fragmentation decay. Further decay of the resulting 187 ion corresponds entirely to the fragmentation pattern noted for the $[M - COOEt]^+$ ion in ester IVa (Table 4).

The N-methylated product of ester Xa, namely, 5-N-methylamino-3-methoxycarbonyl-6-oxo-1-phenyl-1,6-dihydro-1,2,4-triazine (XIa), was isolated as a side product in the above reaction, in 2% yield. The chemical shifts of the phenyl and methoxycarbonyl residue protons in compounds XIa and Xa are practically identical, which is indicative of the presence of a 1,2,4-triazine ring with identical substituents in triazines XIa (and Xa). The spectrum of compound XIa contains, however, a signal for one NH proton and, in addition, a doublet for the N-methyl group protons which are coupled to the other NH proton ($^3J_{H,CH} \approx 5.3$ Hz); these data establish unequivocally both the structure and tautomeric form of the product XIa.

As was observed in the case of the mass spectrum of ester Xa, the characteristic pathway for mass spectral decay of the molecular ion M^+ of ester XIa involves elimination of a methoxycarbonyl group. The m/e values for the Φ_1 and Φ_2 ion peaks are the same, 119 and 91, respectively. The mass number for M^+ is 14 amu higher than in compound Xa. The mass numbers of the $[M - COOR]^+$, $[M - COOR - CO]^+$, Φ_3, and Φ_4 ions are also 14 amu higher in XIa than Xa (Table 4). The combination of these mass spectral data confirms that compound XIa contains a methoxycarbonyl group, just as compound Xa, but that it also has undergone methylation at the amino group as well.

The principal product obtained upon methylation of ester IVa in dimethyl sulfate [7] is 4-N-methyl-5,6-dioxo-1-phenyl-3-ethoxycarbonyl-1,4,5,6-tetrahydro-1,2,4-triazine (XIIa). Its structure was established based on its ^{13}C-NMR spectrum, which contained an N-methyl group signal at δ 32.4 ppm with a $^1J_{CH}$ value of 144 Hz; these values are consistent with data obtained earlier for N-methylated sym-triazines [1]. The fact that methylation has occurred uniquely at the 4-position (and not the 2-position) is supported by the observation of vicinal coupling of the type $^3J_{C(3),CH_3} \approx {}^3J_{C(5),CH_5} \approx 2.6$ Hz. The chemical shift values of the carbon atoms in the triazine and phenyl rings in compound XIIa are similar to the corresponding values in the dioxo derivatives VIIa-IXa, providing additional support for its proposed structure.

The principal mass spectral fragmentation pathways for compound XIIa are similar to the decay pattern observed for compound IXa, which suggests the presence of a 5,6-diketo functional group arrangement. Upon deuteration in a system via direct introduction in the mass spectrometer it was found that molecule XIIa does not contain any active (exchangeable) protons. The atomic mass numbers for M^+ (275) and the $[M - CO]^+$ (247) and $[M - 2CO]^+$ ions (219) are 14 amu higher than than for the corresponding ions in the mass spectrum of ester IXa. This again provides unequivocal evidence for the fact that derivative XIIa is the product of methylation of the NH group.

A monomethyl derivative XIIa was isolated as a side product in the above reaction, in 6% yield; according to its PMR spectrum this derivative is analogous to compound XIa, except that it contains an ethoxycarbonyl substituent rather than a methoxycarbonyl group. When the mass spectrum of XIIIa is compared to that of IVa, it is seen that the m/e values of the M^+, $[M - COOEt]^+$, $[M - COOEt-CO]^+$, Φ_3, and Φ_4 ions are 14 amu higher. Deuteration of compound

XIIIa via direct introduction in the mass spectrometer reveals the presence of one active proton, which is retained in both the Φ_3 and Φ_4 ions (Scheme 2); these data verify that compound XII is the mono-N-methyl derivative of compound IVa.

Upon reaction of triazine I with semicarbazide XIV the 1,2,4-triazine derivative XV was obtained, along with the product isolated in the analogous reaction with acylhydrazines [4]; the 1,2,4-triazine product XV that had previously been incorrectly assigned structure XVI [4]. Detailed analysis of the ^1H- and ^{13}C-NMR spectra of compound XV revealed that this material, namely, 5-amino-6-oxo-3-ethoxycarbonyl-1,6-dihydro-1,2,4-triazine (XV), is an analog of the recyclization product of sym-triazine I with arylhydrazines IIa-f. The PMR spectra of compound XV contain signals for two amino group protons, at δ 7.9 and 8.4 ppm; these values are comprable to the CS of 8.25 and 8.68 ppm observed for the $C_{(5)}-NH_2$ group protons in triazine IVa. A signal at δ 12.9 ppm can apparently be assigned to the $N_{(1)}H$ proton, which is similar in acidity to the protons in barbituric acid derivatives [8], which are also observed downfield. The chemical shifts and SSCC values $^3J_{C_{(6)}NH_A}$ and $^3J_{C_{(6)}NH_B}$ in the ^{13}C-NMR spectrum of compound XV are also similar to the corresponding values for the carbon atoms in the spectrum of compound IVa; these data provide strong support in favor of the proposed structure XV, which can be formed via a mechanism similar to that depicted in Scheme 1. The mass spectrum of compound XV contains an intense molecular ion peak M^+ (184), which undergoes further decay via loss of an ethoxycarbonyl group (139), or $COOC_2H_4$ (112) and CONH (69) species and concomitant formation of the Φ_2 ion.

EXPERIMENTAL

^1H- and ^{13}C-NMR spectra were recorded on a Varian XL-200 spectrometer (at 200 MHz for ^1H and 50.3 MHz for ^{13}C nuclei). TMS was used as internal standard ($\delta_{^1H} = \delta_{^{13}C} = 0$). Electron impact mass spectra and DADI spectra were obtained on an MAT-112 mass spectrometer using direct introduction of the sample into the ion source. The temperature of the ionization chamber was 180°C. The ionizing electron energy was 70 eV. High resolution mass spectra were measured on an MAT-311A mass spectrometer (at a resolution of 15,000). The ionizing electron energy was also 70 eV.* Preparative chromatography was achieved using Chemapol 40/100 μ grade silica gel columns, at a ratio of 1 g substance to be chromatographed to 50 g silica gel.

The results of C, H, N elemental analysis agreed with calculations.

Reaction of 2,4,6-Triethoxycarbonyl-sym-triazine (I) with Phenylhydrazine (IIa). A suspension of 6.15 g (20.6 mmole) triazine I in 50 ml ethanol was refluxed for 2 h with 8.10 g (80.6 mmole) phenylhydrazine IIa. The mixture was cooled and 3.76 g (65%) 5-amino-6-oxo-3-ethoxycarbonyl-1-phenyl-1,6-dihydro-1,2,4-triazine (IVa) was isolated by filtration.

The alcohol mother liquor was evaporated and the residue dissolved in 50 ml benzene. After 24 h 2.09 g (49%) of 1-phenyl-3-ethoxycarbonylamidrazone (Va, $C_{10}H_{13}N_3O_2$), mp 128-130°C (1:1 benzene–heptane), was isolated by filtration. Literature [9] mp 128°C.

(5-Amino-6-oxo-1-phenyl-1,6-dihydro-1,2,4-triazinyl-3)carboxylic Acid (VIa, $C_{10}H_8N_4O_3 \cdot 0.5 H_2O$. To a suspension of 0.7 g (2.7 mmole) aminoester IVa in 190 ml ethanol was added 5.6 ml 0.5 N (2.8 mmole) NaOH solution. The solution was stirred 24 h at 20°C, then acidified with 13.6 ml of 0.5 N hydrochloric acid. Acid VIa (0.61 g, 98%) was removed by filtration. Colorless crystals, soluble in water and hot alcohol solution, mp 239-241°C (dec., from 50% aqueous methanol).

(5,6-Dioxo-1-phenyl-1,4,5,6-tetrahydro-1,2,4-triazinyl-3)carboxylic Acid (VIIa, $C_{10}H_7N_3O_4 \cdot H_2O$). To 2.9 g (15.5 mmole) aminoacid VIa, dissolved in 100 ml hot water, was added 3 ml conc. HCl (pH 2), and the solution was refluxed for 5 min. Acid VIIa was isolated from the cooled solution (2.3 g, 79%). Colorless crystals, soluble in alcohols, acetone, and hot water. The product undergoes decarboxylation at 181-183°C to give a crystalline material with mp 221-222°C.

5,6-Dioxo-1-phenyl-1,4,5,6-tetrahydro-1,2,4-triazine (VIIIa, $C_9H_7N_3O_2$. Dioxo acid VIIa (0.4 g, 1.7 mmole) was held at 180-190°C until no more CO_2 evolution was observed (5 min). The product was cooled and crystallized from isopropyl alcohol. Yield 0.3 g (93% triazine

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VIIIa. Colorless crystals, soluble in acetone, chloroform, and hot alcohols, mp 220-222°C (isopropyl alcohol).

5,6-Dioxo-1-phenyl-3-ethoxycarbonyl-1,4,5,6-tetrahydro-1,2,4-triazine (IXa, $C_{12}H_{11}N_3O_4$). A solution of 0.7 g aminoester IVa in 50 ml aqueous alcoholic HCl solution was refluxed 5 h, until no more starting material remained according to TLC analysis. The solution was evaporated to dryness and the residue refluxed with chloroform (3 × 30 ml) and crystallized from ethyl acetate. Yield 0.6 g (85%) of triazine IXa. Colorless crystals, soluble in chloroform and hot alcohols, acetone and ethyl acetate, mp 208-210°C (ethyl acetate).

Methylation of IVa with Dimethyl Sulfate. A. To a freshly prepared solution of 18 mmoles sodium methoxide in 50 ml methanol and 0.78 g (13 mmoles) aminoester IVa was added with stirring 1.89 g (15 mmoles) dimethyl sulfate. The mixture was refluxed 2 h, allowed to stand an additional 48 h, and the methanol was evaporated. The residue was boiled with chloroform (4 × 50 ml). After evaporation of the chloroform solvent the residue was transferred to a column. Elution with benzene–ethyl acetate (4:1) gave first of all 0.02 g (2%) 5-N-methylaminotriazine XIa (colorless crystals, soluble in chloroform, ethyl acetate, and acetone; mp 204-205°C from 1:1 hexane–benzene), followed by 0.22 g (30%) of methyl ester Xa, whose solubility was similar to that of triazine IVa. mp 239-241°C (ethanol).

B. A suspension of 1 g (3.8 mmole) aminoester IVa in 1 ml (9.5 mmole) dimethyl sulfate was stirred and heated at 135-145°C for 10 min. The reaction mixture became homogeneous upon heating. The mixture was cooled, 15 ml water was added, and after 30 min the product was extracted with chloroform (3 × 20 ml). The chloroform solution was dried over potash, evaporated, and the residue was transferred to a silica gel column. Elution with a mixture of benzene–ethyl acetate (5:1) gave 0.25 g of triazine XIIa ($C_{13}H_{13}N_3O_4$). Colorless crystals, soluble in chloroform, ethyl acetate, acetone, hot benzene, and alcohols. mp 114-115°C (heptane–benzene, 1:1).

Further elution with the same solvent mixture gave 0.06 g (6%) 5-N-methylamino derivative XIIIa. Colorless crystals, mp 164-165°C (hexane–benzene, 1:1).

From the original aqueous solution was recovered by precipitation after 24 h an additional 0.25 g of triazine XIIa. Total yield of the latter, 0.5 g (47%).

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