MANGANESE DIOXIDE OXIDATION OF HYDROXYAMINO-*sym*-TRIAZINES*

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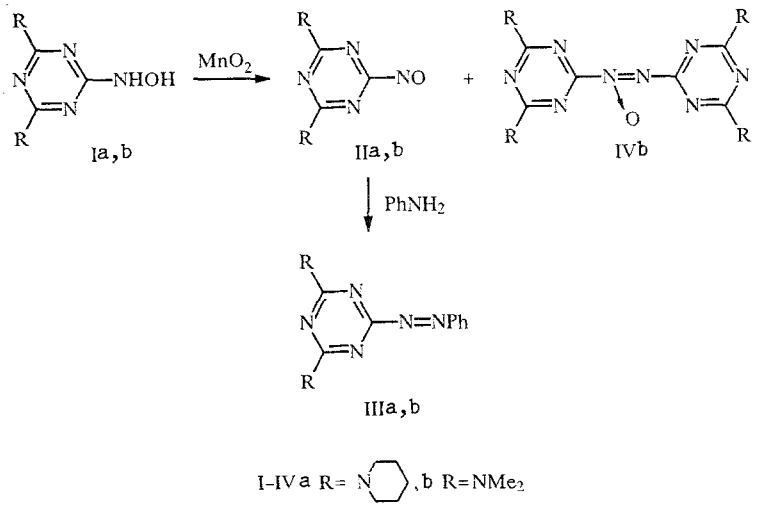
The hydroxyamino group in sym-*triazines is readily oxidized by the action of manganese dioxide. The stability of the nitrosotriazines formed in this oxidation depends on the electron donor properties of the other substituents in the molecule.*

In previous work [2-4], we showed that the oxidation of alkyl and aryl derivatives of hydroxyaminopyrimidines leads to the corresponding nitroso, nitro, and azoxy derivatives depending on the nature of the oxidizing agent. In a continuation of a study of the effect of six-membered nitrogen heterocycles on the chemical transformations of the hydroxyamino group, we investigated the oxidation of this group in substituted *sym*-triazines. In the present work, data are given on the behavior of 2-hydroxyamino-4,6-R_2-*sym*-triazines (Ia-Id) with electron-donor substituents upon the action of activated manganese dioxide. Electron donor substituents were selected in order to achieve partial compensation for the electron-withdrawing effect of the oxygen-containing nitroso or azoxy groups, whose formation would be expected under the oxidation conditions studied [3]. This would lead to an increase in the stability of these triazine derivatives. Prior to this work, nitroso- and azoxy-*sym*-triazines had not been reported [1].

Oxidation of 2-hydroxyamino-3,6-dipiperidino-*sym*-triazine (Ia) in chloroform using activated MnO_2 led to 2-nitroso-4,6-dipiperidino-*sym*-triazine (IIa), which is stable at room temperature. This conclusion was supported by chemical analysis and IR and UV spectral data. The greenish color of the solution of IIa in chloroform is characteristic for the mono-meric form of nitrosoazines [5]. The reaction of IIa with aniline gives 4,6-dipiperidino-2-phenylazo-*sym*-triazine (IIIa).



The oxidation of 2-hydroxyamino-4,6-bis(dimethylamino)-*sym*-triazine (Ib) under analogous conditions leads to the formation of a mixture of 2-nitroso- (IIb) and 2-azoxy-4,6-bis(dimethylamino)-*sym*-triazines (IVb). Product IIb also reacts with aniline to give 4,6-bis(dimethylamino)-2-phenylazo-*sym*-triazine (IIIb). The structure of azoxy derivative IVb was

*For previous Communication, see [1].

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TABLE 1. Mass Spectra of Ia, Ib, IIa, and IIb

Compound	m/z (I_{rel}, %)*
Ia	279 (17), 278 (100) $[M]^{+\cdot}$, 261 (22), 249 (16), 233 (7), 195 (6), 136 (14), 111 (10)
IIa	278 (2) $[M+2]^+$, 247 (10), 246 (68) $[M-NO]^+$, 163 (6), 137 (8), 136 (100)
Ib	199 (10), 198 (100) $[M]^{+\cdot}$, 184 (35), 183 (10), 169 (8), 168 (10), 167 (9), 166 (5), 155 (6), 152 (8), 139 (10), 138 (32), 111 (6)
IIb	198 (5) $[M+2]^+$, 167 (20), 166 (100), $[M-NO]^+$, 107 (14)

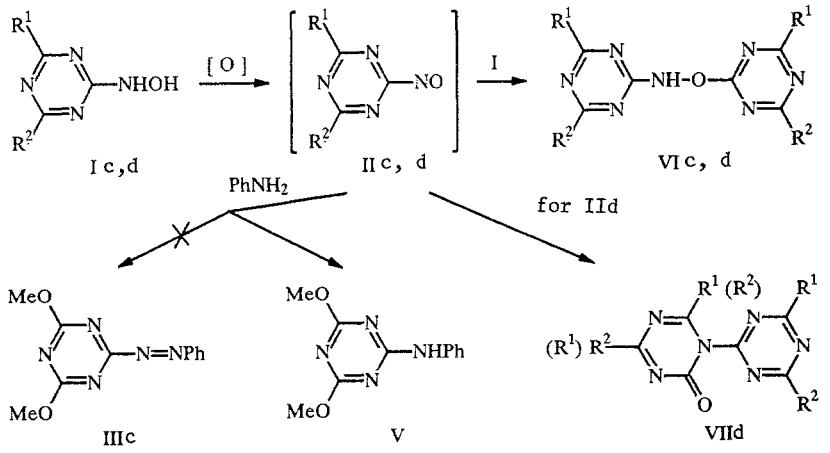
*The ions with *m/z* greater than 100 and intensity greater than 5% are given.

indicated by analytic data, its PMR spectrum, which has three types of signals of N-methyl group protons (Table 2), and its high-resolution mass spectrum* taken at 120°C ($[M]^+$ 376, 2193). At higher temperatures, this compound is unstable and readily loses a nitrogen molecule to give an ion with *m/z* 348, 2143 $[M-28]^+$ (see our previous work [2]).

Nitroso compounds IIa and IIb do not give molecular ions in their mass spectra, but rather only ions with *m/z* $[M+2]^+$ (278 for IIa and 198 for IIb) and strong fragment ions $[M-NO]^+$ (246 for IIa and 166 for IIb). The formation of such ions in the mass spectrometer has been observed for other nitrosoazines, namely, pyrimidines [3] and quinolines [6]. The lack of traces of starting compounds Ia and Ib in products IIa and IIb was indicated by a negative $FeCl_3$ test, thin-layer chromatography data, and the difference in the mass spectra of I and II (Table 1). Clarification of the reason for the appearance of the $[M+2]^+$ peak requires further study.

The oxidation of 2-hydroxyamino-4,6-dimethoxy-*sym*-triazine (Ic) also led to solutions with a color characteristic for nitrosoazines but the corresponding nitrosoazine IIc could not be isolated. This failure indicates that this product is unstable. In order to establish the formation of 4,6-dimethoxy-2-nitroso-*sym*-triazine (IIc), the reaction mixture was treated with aniline immediately after the oxidation of Ic. However, the expected product, 4,6-dimethoxy-2-phenylazo-*sym*-triazine (IIIc), was not detected. 4,6-Dimethoxy-2-phenylamino-*sym*-triazine (V) was isolated from the complex product mixture. The formation of amino derivative V may be related to two competing reactions for nitrosoazines, namely, nucleophilic substitution of the nitroso group and reaction of the nitroso group with amines to give azo derivatives. The rate of the nucleophilic substitution in the case of IIc is probably much greater than the rate of formation of the azo compound. Similar behavior of a nitroso group relative to aniline has been reported for 2,4,6-trinitro-1-nitrosobenzene [7], for which nucleophilic substitution of the nitroso group by hydroxy and alkoxy groups was also described [7].

A compound corresponding to $C_{10}H_{13}N_7O_5$ (VIc) was isolated from the reaction mixture after the oxidation of Ic by activated MnO_2 and the presence of 2-hydroxy-4,6-dimethoxytriazine (VIII) was indicated by mass spectrometry. The IR spectrum of VIc has an NH stretching band at 3370 cm^{-1}, while the PMR spectrum shows that the two triazine fragments in



I, II, VI, VII c $R^1 = R^2 = OMe$; d $R^1 = OMe$, $R^2 = NMe_2$

*Here and below, the *m/z* values are given.

TABLE 2. Indices of Compounds Synthesized

Compound	Chemical formula	M^+ found / calculated	mp, °C	UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	PMR spectrum, δ, ppm (in $CDCl_3$)	Yield, %
Ia	$C_{13}H_{22}N_6O$	278	205...208 [12]	—	—	80
Ib	$C_7H_{14}N_6O$	198	195...198 (dec.)	—	—	60
Ic	$C_5H_8N_4O_3$	172	174...176 [13]	—	—	90
Id	$C_6H_{11}N_5O_2$	185	193...195 (dec.)	—	—	82
IIa	$C_{13}H_{20}N_6O$	—	181...184 (dec.)	234 (48), 320 (5,3)	—	30
IIb	$C_7H_{12}N_6O$	—	171...174 (dec.)	230 (39), 316 (4,8)	—	35
IIIa	$C_{19}H_{25}N_7$	351,2170 / 351,2171	155...157	233 (43,5), 292 (14)	—	90
IIIb	$C_{13}H_{17}N_7$	271,1524 / 271,1545	114...115	228 (33), 292 (7,9)	3,17 (12H, s, N—CH_3), 7,33...7,58 (3H, m, H_{arom}), 7,83...8,10 (2H, m, H_{arom}),	60
IVb	$C_{14}H_{24}N_{12}O$	376,2193 / 376,2196	243...245	231 (66)	3,13 (12H, s), 3,15 (6H, s), 3,20 (6H, s, N—CH_3)	30
V	$C_{11}H_{12}N_4O_2$	232,0931 / 232,0960	131...133 [14]	—	—	20
VIc	$C_{10}H_{13}N_7O_5$	311,0946 / 311,0978	174...177	216 (18)	3,90 (6H, s, OCH_3), 3,98 (6H, s, OCH_3)	50
VId	$C_{12}H_{19}N_9O_3$	337,1614 / 337,1611	194...198	230 (39)	3,16 (12H, s, N—CH_3), 3,85 (3H, s, OCH_3), 3,89 (3H, s, OCH_3)	30
VIId	$C_{12}H_{18}N_8O_3$	322,1541 / 322,1502	206...208	214 (22), 238 (39)	3,141, 3,171 (6H, 2 s, N—CH_3), 3,190, 3,194 (6H, 2s, N—CH_3), 3,917 (3H, s, OCH_3), 3,938 (3H, s, OCH_3)	25

the molecule are not equivalent (Table 2). This led us to identify the product as N,O-bis(4,6-dimethoxytriazinyl-2)hydroxylamine (VIc). The formation of this compound as well as of V and VIII is probably related to the enhanced nucleophilic lability of the nitroso group in the triazine ring and its rapid replacement upon formation by the nucleophile present in the reaction medium. The hetarylation of monosubstituted hydroxylamine Ic proceeds at the oxygen atom as has been reported for similar compounds with electron-withdrawing substituents at the nitrogen atom of the hydroxyamino group [8, 9].

The oxidation of 2-hydroxyamino-4-dimethylamino-6-methoxy-*sym*-triazine (Id) proceeds analogously to the oxidation of Ic and two compounds were isolated from the reaction mixture. The compound with the formula $C_{12}H_{19}N_9O_3$ and spectral data similar to those for VIc corresponds to N,O-bis(4-dimethylamino-6-methoxytriazinyl-2)hydroxylamine (VId). The other compound with formula $C_{12}H_{18}N_8O_3$ has an IR band at 1720 cm^{-1} (ν_{CO} for cyclic amide) and does not display an NH stretching band. The PMR spectrum of this compound has a set of signals indicating that the two triazine rings are not equivalent, namely, that there are two methoxy groups and four $N-CH_3$ groups. The methyl protons in both dimethylamino groups are magnetically inequivalent due to hindrance to free rotation of these groups about the exocyclic C–N bonds and two pairs of singlets are observed with separation of 0.004 and 0.030 ppm. Warming the sample to 40°C leads to coalescence of the pair of dimethylamino group signals, characteristic for dialkylaminotriazines, and broadening of the pair of signals of the second dimethylamino group. Coalescence of this latter pair of signals occurs above 55°C (Fig. 1). Behavior analogous to that of the second dimethylamino group was observed by Dovlatyan et al. [10] in the PMR spectrum of 2-dimethylamino-4-oxo-6,7-dihydro-4H-oxazolo[3,2-*a*]-*sym*-triazine in $CDCl_3$ at different temperatures. These findings suggest that the compound obtained has an N-substituted oxodihydrotriazine fragment and permitted us to identify it as N^e-(4-dimethylamino-6-methoxy-triazinyl-2)-4(6)-dimethylamino-6(4)-methoxy-2-oxo-1,2-dihydrotriazine (VIId). The formation of this compound may proceed through an unstable azoxy intermediate by analogy to the thermal decomposition of azoxypyrimidines [2] or through nitrosotriazine IId by analogy with the transformation of 2-nitrosopyridines to the corresponding N-(pyridyl-2)-pyridones-2 [11].

A study of the behavior of substituted hydroxyaminotriazines upon the action of MnO_2 indicates that the oxidation of the hydroxyamino group in *sym*-triazines proceeds quite readily, while the stability of the nitroso products depends on the electron donor properties of the other substituents in the molecule. Two piperidino groups provide the greatest stabilization (Ia), while two methoxy groups provide slight stabilization (Ic).

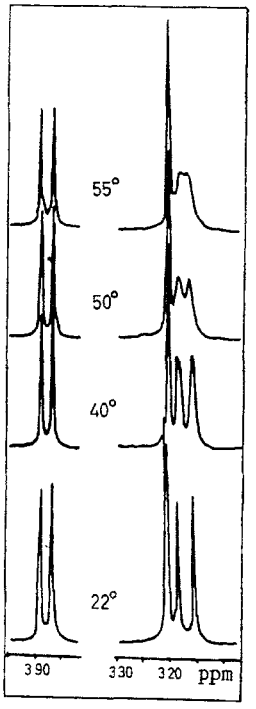


Fig. 1. PMR spectra of compound VIId in $CDCl_3$ at room temperature.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer for KBr pellets or chloroform solutions. The UV spectra were taken on a Specord UV-VIS spectrometer for ethanol solutions. The PMR spectra were taken on Varian A56/60 (IIIb, VIc, and VId) and WP-200 spectrometers (IVb and VIId). The mass spectra were taken on a Finnigan MAT-8200 mass spectrometer. The M^+ values were determined by high-resolution mass spectrometry. The purity of the compounds was checked by thin-layer chromatography on Silufol UV-254 plates using chloroform as the eluent. Catalytic manganese(IV) oxide (TU 6-09-37) was used for the oxidation. The yields, melting points, and spectral data of the synthesized products are given in Tables 1 and 2.

The elemental analysis for C, H, and N corresponded to the calculated values.

Hydroxyamino-*sym*-triazines Ia-Id. A saturated solution of sodium carbonate in 50% aqueous methanol was added to a saturated solution of hydroxylamine hydrochloride in methanol and the precipitate was filtered off. A solution of 2-chloro-4,6-R^2-*sym*-triazine in methanol was added to the filtrate (the $NH_2OH \cdot HCl - Na_2CO_3$ – triazine mole ratio was 3:1.5:1). In the preparation of Ic, the starting chlorotriazine reacted completely at room temperature in 10 min. In the preparation of the other hydroxyaminotriazines, the reaction mixture was heated at reflux for 3-9 h until the starting chlorotriazine disappeared. In order to isolate Ia and Ib, the precipitate formed was filtered off, washed with water, and recrystallized from methanol.

In order to isolate Ic and Id, the reaction mixture was evaporated. The residue was treated with water and filtered. The precipitate was recrystallized from methanol.

2-Nitroso-4,6-dipiperidino-*sym*-triazine (IIa). A suspension of 1.7 g MnO_2 in 40 ml chloroform was stirred at room temperature for 15 min. A sample of 0.28 g (1 mmole) hydroxyaminotriazine Ia was added and the mixture was stirred for 1 h. The precipitate was filtered off and washed with 20 ml chloroform. Then chloroform was evaporated and the residue was recrystallized from ethyl acetate to give 0.08 g nitrosotriazine IIa.

4,6-Bis(dimethylamino)-2-nitroso-*sym*-triazine (IIb) and 2-Azoxy-4,6-bis(dimethylamino)-*sym*-triazine (IVb). Triazine Ib was oxidized analogously to Ia. After evaporation of chloroform, the residue was recrystallized from ethyl acetate to give 0.07 g nitrosotriazine IIb. The mother liquor was evaporated and the residue was subjected to chromatography on a silica gel column using 4:1 chloroform–acetone as the eluent to give 0.06 g azoxytriazine IVb (from ethyl acetate).

4,6-Bis(dimethylamino)-2-phenylazo-*sym*-triazine (IIIb). A sample of 0.2 g (2 mmoles) aniline and 0.1 ml acetic acid were added to a solution of nitrosotriazine IIb in chloroform obtained as described above from 1.0 mmole Ib and stirred at room temperature for 48 h. The mixture was evaporated and the residue was subjected to chromatography on a silica gel column using chloroform as the eluent to give 0.16 g azo derivative IIIb (from petroleum ether, bp 40-70°C). Then elution with 4:1 chloroform–acetone gave 0.06 g azoxytriazine IVb.

4,6-Dipiperidino-2-phenylazo-*sym*-triazine (IIIa) was obtained analogously to IIIb.

4,6-Dimethoxy-2-phenylamino-*sym*-triazine (V) was obtained analogously to the procedure described above for IIIb. The product mixture after evaporation of chloroform was subjected to chromatography on a silica gel column with chloroform–acetone as the eluent to give 0.05 g V (from ethanol).

N,O-Bis(4,6-dimethoxytriazinyl-2)hydroxylamine (VIc). A suspension of 1.7 g MnO_2 in 40 ml chloroform was stirred at room temperature for 15 min and 0.17 g (1 mmole) triazine Ic. This mixture was stirred for 1 h. The precipitate was filtered off and washed with 20 ml chloroform. After evaporation of the solvent, the precipitate was triturated with 20 ml ether and left overnight. The precipitate was filtered off and recrystallized from ethyl acetate to give 0.08 g VIc. IR spectrum, ν: 3280 and 3345 (KBr), 3370 cm^{-1} ($CHCl_3$). Products VIc ($[M]^{+\cdot}$ 311) and VIII ($[M]^{+\cdot}$ 157) precipitated out from the filtrate.

N,O-Bis(4-dimethylamino-6-methoxy-*sym*-triazinyl-2)hydroxylamine (VId) and N'-(4-dimethylamino-6-methoxy-*sym*-triazinyl-2)-4(6)-dimethylamino-6(4)-methoxy-2-oxo-1,2-dihydro-*sym*-triazine (VIId). The oxidation of 1.0 g (5.4 mmoles) Id by 9.0 g MnO_2 was carried out analogously to the procedure for Ic and gave 0.6 g precipitate. Purification of the precipitate by preparative thin-layer chromatography on Silufol plates using 4:1 chloroform–acetone as the eluent gave 0.27 g bis-triazinylhydroxylamine VId and 0.22 g triazinone VIId (from ethanol). IR spectrum, ν: For VId 3275 and 3340 (KBr), 3350 cm^{-1} ($CHCl_3$); for VIId 1715 cm^{-1} (C=O) (KBr).

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