GEMINAL SYSTEMS.

13.* SYNTHESIS AND AMINOAMINATING ABILITY OF N,N-DI-tert-ALKYL-N'-ALKOXYDIAZENIUM SALTS

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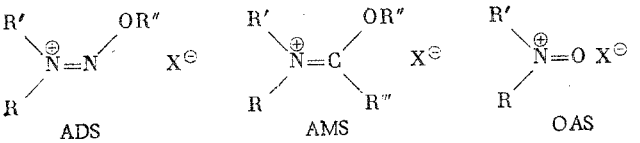
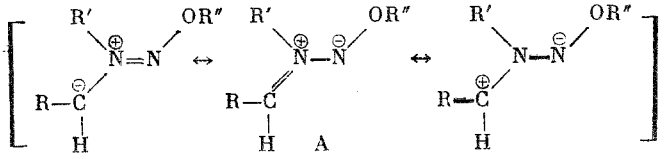
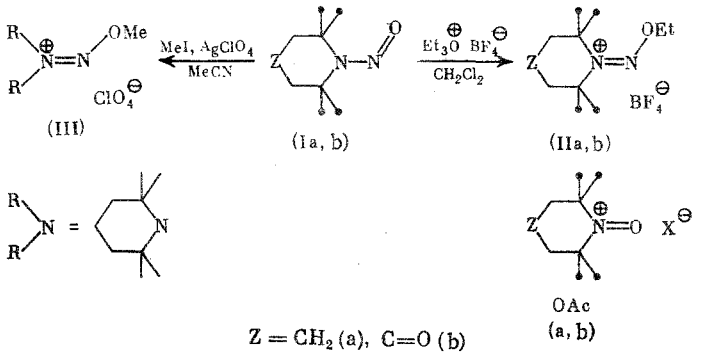
Alkoxydiazenium (nitrosoamidium) salts (ADS) can be regarded as being the aza analogs of alkoxymethylenimmonium (amidium [2]) (AMS) and oxammonium salts (OAS), for which the aminomethylation [3] and aminooxylation [4] of nucleophiles are characteristic reactions. Consequently, a study of the aminoaminating ability of ADS is of interest.



The previously known ADS contain a proton α to either the R or R' substituent and react differently with nucleophiles, and specifically via the intermediate formation of dipole (A), which then acts as a C-electrophile [5].



In this connection it was proposed to effect the aminoamination of nucleophiles using ADS (IIa, b) and (III), with tert-alkyl substituents R and R', which were obtained from the corresponding nitrosamines (Ia, b) as described in [6] (Scheme 1).



The barrier of rotation around the C=N bond in the AMS is ∿20 kcal/mole [2]. Our attempts to determine the barrier of rotation around the N=N bond in ADS (IIa) and (III) by the DNMR method on the basis of the merging temperature of the signals of the nonequivalent 2-Me_2 and 6-Me_2 groups (Table 1) proved unsuccessful due to the low heat stability of the compounds: vigorous decomposition with the evolution of N_2 is observed at 80°C in $PhNO_2$.

In their relative heat stability the ADS (IIa, b) and (III) are close to their isoelectronic OAS analogs (a, b, $X^{\ominus} = Cl^{\ominus}$) [7]. In the crystalline state both (IIa) and (III) are completely stable when stored in a dry atmosphere for a month at 20°, whereas (IIb) de-

*See [1] for Communication 12.

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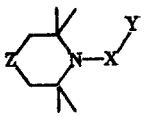
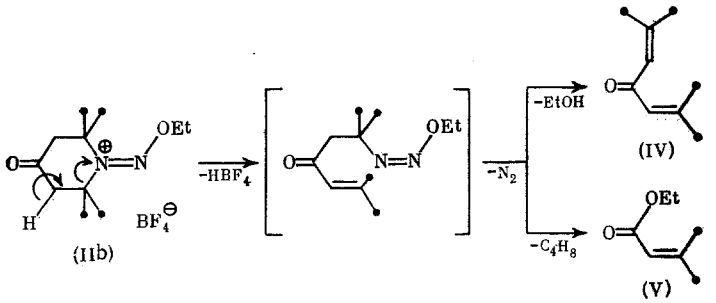
TABLE 1. Parameters of PMR and UV Spectra of 2,2,6,6-Tetramethylpiperidine Derivatives



Compound	X	Y	Z	PMR spectrum, δ, ppm, J, Hz				UV spectrum (in MeOH)	
				2,2,6,6-Me_4	CH_2 of ring	Y	sol-vent	λ_{max}, nm	log ε
(Ia)	N	O	CH_2	1,34 & 1,53	1,75 m		CD_3OD	237	3,82
(Ib)	N	O	CO	1,42 & 1,65	2,70 & 2,73		CD_3OD	232	3,82
(IIa)	N	OEt	CH_2	1,63 & 1,65	1,96 m	1,54 t (Me, J=7,5), 5,15 q (CH)	CD_3OD	229	3,80
				1,73 & 1,75	2,12 m	1,62 t (Me, J=7,5), 5,33 q (CH_2)	$PhNO_2$		
(IIb)	N	OEt	CO	1,70 & 1,75	3,02 & 3,15	1,59 t (Me, J=7,5), 5,23 q (CH_2)			
(III)	N	OMe	CH_2	1,61 & 1,64	2,01 m	4,78 (MeO)	CD_3OD	227	3,94
				1,73 & 1,76	2,10 m	5,03 (MeO)	CD_3OD	229	3,66
(VI)	N	OEt	CH_2	1,63 & 1,65	1,96 m	1,54 t (Me, J=7,5), 5,15 q (CH_2)	CD_3OD	229	—
(VII)	N	NMe	CH_2	1,25	1,50	3,25 (MeN)	CCl_4	—	—
(VIII)	N	CHCOOMe	CH_2	1,27	1,59	3,61 (MeO), 6,74 (CH)	CCl_4	282	4,42

composed with explosive force in a vacuum desiccator at the same temperature. From the decomposition products were isolated phorone (IV) and β,β-dimethylacrylic ester (V). The easy decomposition of (IIb) is apparently caused by the lability of the protons of the CH_2CO group.

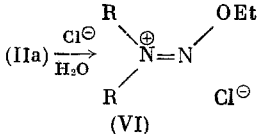


(IIb) (IV) (V) (2)

The intermediate formation of the azo compound is confirmed by the fact that the decomposition of OAS (b), $X^{\ominus} = CCl_3COO^{\ominus}$, gave a structurally similar nitrosoalkane [8].

The stability of the ADS also depends on the nucleophilicity of the anion. The chromatographing of tetrafluoborate (IIa) on anionite Dowex 21K (as the Cl^- form) gave the unstable chloride (VI), which decomposes rapidly at 20° with the evolution of N_2.

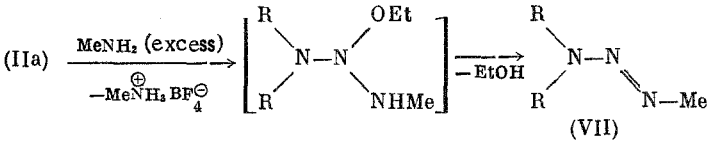
From the identical nature of the PMR and UV spectra of chloride (VI) and its precursor (IIa) (see Table 1) it follows that the N–Cl bond in (VI) has a purely ionic character. In N-chloro-N-alkoxyamines this bond is covalent, as is evidenced by their high configurational stability [9].



(VI) (3)

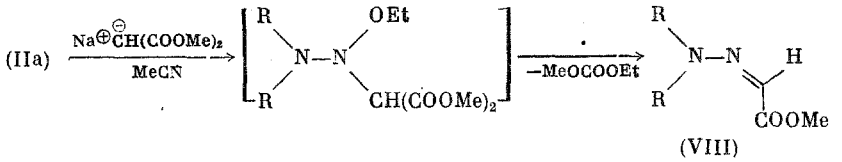
As a result, an increase in the +M effect of the substituents on the N atom in heterosubstituted N-haloamines facilitates the ionization of the N–Hal bond.

The reaction of tetrafluoborate (IIa) with $MeNH_2$ does not lead to the expected N-ethoxy-N-aminohydrazine, but only to the product of its subsequent transformation, namely triazene (VII).



(4)

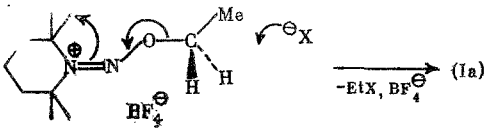
When (IIa) is reacted with dimethyl sodiomalonate, we isolated, instead of N-ethoxyhydrazine, its unusual decomposition product (VIII), with the elimination of MeOCOOEt.



(5)

The cleavage of EtOH could be postulated when a labile malonic proton is present, both on the basis of Scheme (4) and by analogy with the reaction of N,N-dimethyl-N'-methoxydiazenium methosulfate with sodium cyclopentadienyl [10].

In reactions (4) and (5) we isolated, together with triazene (VII) and hydrazone (VIII), also nitrosamine (Ia) in respective yields of 59 and 33%. This can be explained by the competitive attack of the nucleophile on the carbon atom of the Et group. In other words, ethylation of the nucleophile occurs, i.e., (IIa) functions as an alkylating agent. Predominant attack on the C atom in ADS (IIa) is realized using alcoholates (MeONa in MeOH and t-BuONa in glyme) and Me_2NH in MeCN, and here nitrosamine (Ia) was obtained in 75-95% yields. Compound (Ia) was isolated in only 9.4% yield when (IIa) is reacted with MeMgI in ether.

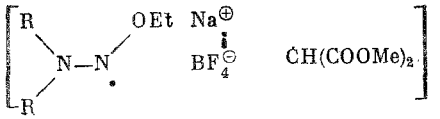


(6)

$X^{\ominus} = MeNH_2$, Me_2NH, $MeO^{\ominus}$, $t\text{-}BuO^{\ominus}$, $(MeOOC)_2\overset{\ominus}{C}H$, MeMgI.

A similar reaction is known for N-phenyl-N-methyl-N'-methoxydiazenium tetrafluoborate, which under the influence of NaI gives MeI [11].

By analogy with the reactions of OAS (a) [12] it could be postulated that one-electron transfer is possible in the reactions of ADS (IIa) with nucleophiles, for example, with dimethyl sodiomalonate, to give the following radical pair:



However, when reaction (5) (0.01 M solution in MeCN) was run in the resonator of an EPR spectrometer, the indicated ethoxyhydrazyl radical cannot be recorded. This can be due either to its low stability or the ionic mechanism of the reaction.

It was shown by model experiments that nitrosamine (Ia) is inert under the conditions of reactions (4) and (5), which excludes the possible formation of (VII) and (VIII) via the dealkylation of (IIa) and subsequent reaction of (Ia) with $MeNH_2$ and dimethyl sodiomalonate. As a result, reactions (4) and (5) can serve as reliable proof of the aminoaminating ability of ADS.

EXPERIMENTAL

The PMR spectra were obtained on a Tesla BS-487C spectrometer (80 MHz, internal standard = HMDS), the UV spectra were obtained on a Specord UV-Vis spectrophotometer, and the mass spectra were obtained on an MX-1303 spectrometer, equipped with a cylinder system of admission at 30 eV, and on a Jeol JMS-01SG-2 high-resolution spectrometer, with direct insertion of the sample into the ion source at 70 eV.

1-Nitroso-2,2,6,6-tetramethylpiperidine (Ia). With stirring, to a solution of 33.10 g (0.186 mole) of 1,1,6,6-tetramethylpiperidine hydrochloride in 100 ml of water was added a solution of 41.40 g (0.60 mole) of $NaNO_2$ in 50 ml of water. After keeping for 2 days the

mixture was refluxed for 7 h, extracted with ether (3 × 50 ml), and dried over $MgSO_4$. After evaporation of the solvent the residue was vacuum-distilled to give 22.26 g (70.3%) of (Ia) (see Table 1) with bp 64-65°C (0.6 mm), mp 16°, cf. [13]. Mass spectrum (30 eV), m/e (rel. intensity, %): M^+ 170(31), 140(47), 125(16), 109(7), 97(33), 84(22), 69(100), 56(60), 41(42).

1-Nitroso-2,2,6,6-tetramethyl-4-piperidone (Ib). With stirring, to a solution of 20.18 g (0.13 mole) of 2,2,6,6-tetramethyl-4-piperidone in 100 ml of water at 10-15° was added 13 ml (∿0.15 mole) of 36% aqueous HCl solution, and then at 0-3° was added a solution of 10.35 g (0.15 mole) of $NaNO_2$ in 20 ml of water. The stirring was continued for 1 h and the mixture was let stand for 24 h at 0°. The product was extracted with ether (3 × 50 ml) and dried over $MgSO_4$. After removal of the ether the residue was vacuum-sublimed at 60-70° (0.5 mm) to give 13.73 g (57.3%) of (Ib) with mp 73°, cf. [14]. Mass spectrum (30 eV), m/e (rel. intensity, %): M^+ 184(9), 140(9), 128(13), 110(6), 98(9), 83(15), 70(11), 56(100).

1-Ethoxyimino-2,2,6,6-tetramethylpiperidinium Tetrafluoborate (IIa). With stirring, to a solution of 21.77 g (0.115 mole) of $Et_3O^{\oplus}BF_4^{\ominus}$ in 70 ml of abs. CH_2Cl_2 at 0° was added in drops a solution of 20.43 g (0.12 mole) of (Ia) in 30 ml of abs. CH_2Cl_2. After keeping for 30 min at 0° the solvent was evaporated in vacuo. The residue was recrystallized from abs. MeOH to give 28.68 g (87.2%) of (IIa) with mp 81° (decompn.). Found: C 46.11; H 8.08; N 9.87%. $C_{11}H_{23}N_2OBF_4$. Calculated: C 46.18; H 8.10; N 9.79%.

1-Ethoxyimino-2,2,6,6-tetramethyl-4-oxopiperidinium Tetrafluoborate (IIb). With stirring, to a solution of 8.45 g (0.045 mole) of $Et_3O^{\oplus}BF_4^{\ominus}$ in 20 ml of abs. CH_2Cl_2 at 0-5° was added in drops a solution of 9.21 g (0.05 mole) of (Ib). After 5 min (5-10°) the mixture was cooled to −60 to −70° and the obtained crystals were filtered and washed with ether to give 11.00 g (73.2%) of (IIb) with mp 75° (decompn.). Found: C 44.15; H 7.16; N 9.39%. $C_{11}H_{21}N_2O_2BF_4$. Calculated: C 44.02; H 7.05; N 9.33%.

1-Methoxyimino-2,2,6,6-tetramethylpiperidinium Perchlorate (III). With stirring and cooling, to a solution of 1.70 g (0.01 mole) of (Ia) and 1.56 g (0.011 mole) of MeI in 10 ml of abs. MeCN was added a solution of 2.07 g (0.01 mole) of $AgClO_4$ in 10 ml of MeCN and the mixture was let stand overnight at 0°. After removal of the precipitate the filtrate was evaporated in vacuo and the residue was recrystallized from a MeOH–ether mixture to give 2.60 g (91.2%) of (III) with mp 77° (decompn.). Found: C 42.22; H 7.31; N 9.78%. $C_{10}H_{21}NO_5Cl$. Calculated: C 42.18; H 7.43; N 9.84%.

The spontaneous decomposition of 9.6 g of (IIb) leads to a dark red oil, which was dissolved in 50 ml of ether, washed with 10% aqueous $NaHCO_3$ solution, and dried over $MgSO_4$. After removal of the ether and fractional distillation in vacuo we obtained 0.18 g of β,β-dimethylacrylic ester (V) with bp 30-32° (5 mm), cf. [15], and 0.43 g of phorone (IV) with bp 68-70° (5 mm), n_D^{20} 1.4998, cf. [16]. PMR spectra (δ, ppm, in CCl_4): (V) — 1.16 t (Me, J = 7.0 Hz), 1.79 and 2.05 (Me, $J_{trans} = J_{cis} = 1.3$ Hz), 3.95 (CH_2), 5.45 sept. (CH); (IV) — 1.78, 1.83, 1.98 and 2.04 (Me, $J_{trans} = J_{cis} = 1.4$ Hz), 5.62 and 5.80 d. sept. (CH).

1-Ethoxyimino-2,2,6-6-tetramethylpiperidinium Chloride (VI). A solution of 2.1 g (0.0073 mole) of (IIa) in 15 ml of distilled water was passed through an ion-exchange column (d = 1 cm, 16.2 g of anionite Dowex 21K × 50/100 mesh as the $Cl^{\ominus}$ form, H_2O). The eluate (∿80 ml), collected in a cooled receiver (5-3°), was evaporated in vacuo, dissolved in 30 ml of abs. i-PrOH, and dried at 0 to −2° over Wolfen–Zeosorb 4-Å zeolite. After removal of the i-PrOH in vacuo we obtained 1.05 g (61.4%) of (VI) as an oil. Found: Cl 14.61%. $C_{11}H_{23}ClN_2O$. Calculated: Cl 15.10%.

Reaction of (IIa) with Methylamine. A solution of 5.72 g (0.02 mole) of (IIa) in 20 ml (0.45 mole) of $MeNH_2$ was stirred for 1 h at −10 to −15° and then let stand at 20° to remove the $MeNH_2$. The products were extracted from the residue with abs. ether and the ether was evaporated in vacuo to give 3.31 g of a mixture of (Ia) and (VII) in a 62.6:37.4 ratio (based on the PMR spectrum). Distillation gave 1.19 g (32.5%) of (VII) (characterized by the PMR spectrum, see Table 1, the mass spectrum, and conversion to 2,2,6,6-tetramethylpiperidine hydrochloride, see below) with bp 68-72° (10 mm), and 2.01 g (59.1%) of (Ia) with bp 112-113° (10 mm). Mass spectrum of (VII) (30 eV), m/e (rel. int., %): M^+ 183(2), 141(13), 140(8), 126(100), 109(9), 84(23), 69(26), 58(13), 43(26).

A solution of 0.67 g of (VII) in 3 ml of abs. ether was saturated with dry HCl, and the precipitate was filtered and recrystallized from a MeCN–MeOH mixture to give 0.27 g of

2,2,6,6-tetramethylpiperidine hydrochloride with mp above 250°. Found: C 60.99; H 11.38; N 7.93%. $C_9H_{20}ClN$. Calculated: C 60.83; H 11.34; N 7.88%. PMR spectrum (δ, ppm, in $CDCl_3$): 1.54(Me_4), 1.66[$(CH_2)_3$], 8.80($\overset{\oplus}{N}H_2$).

Reaction of (IIa) with Dimethyl Sodiomalonate. To a solution of 0.46 g (0.02 mole) of Na metal in 30 ml of abs. MeOH was added 2.64 g (0.02 mole) of dimethyl malonate, and the MeOH was removed in vacuo. The dry residue was dissolved in 50 ml of abs. MeCN and to the stirred and cooled (–10 to –15°) solution was added in drops 5.72 g (0.02 mole) of (IIa) in 30 ml of abs. MeCN. The stirring was continued for 1 h at 20° and, after keeping overnight, the solvent was removed in vacuo, while the products were extracted from the residue with abs. ether. After removal of the ether we obtained 4.16 g of a mixture of (Ia):(VIII) = 28.6:71.4 (based on the PMR spectrum), which was separated by fractional sublimation in vacuo (0.25 mm). We obtained 1.12 g (33.0%) of (Ia) with mp 16°, and 2.30 g (51.0%) of (VIII) with mp 79-80°. Found: C 63.61; H 9.87; N 12.47%. $C_{12}H_{22}N_2O_2$. Calculated: C 63.68; H 9.86; N 12.38%. Mass spectrum of (VIII) (30 eV), m/e (rel. int., %): M^+ 226(41), 211(100), 195(10), 179(10), 167(10), 155(14), 143(59), 125(9), 109(53), 103(19), 83(34), 69(66), 57(21), 56(47), 42(16).

(VIII) Hydrochloride: mp 118-119° (from EtOAc–ether). Found: C 54.57; H 8.72; N 10.69%. $C_{12}H_{23}ClN_2O_2$. Calculated: C 54.85; H 8.82; N 10.66%. PMR spectrum (δ, ppm, in $CDCl_3$): 1.44 (Me_4), 1.44-2.45 m (CH_2), 3.86 (MeO), 9.23 (CH).

Reaction of (IIa) with Sodium Methoxide. With stirring and cooling (–20 to –25°), to a solution of 0.51 g (0.022 mole) of Na metal in 30 ml of abs. MeOH was added in drops a solution of 5.72 g (0.02 mole) of (IIa) in 40 ml of abs. MeOH. After stirring for 5 h at 20° the solvent was evaporated in vacuo, the product was extracted from the residue with abs. ether, and the ether was evaporated in vacuo. Distillation gave 2.54 g (74.7%) of (Ia) with bp 64-65° (0.6 mm).

Reaction of (IIa) with Sodium tert-Butoxide. With stirring and cooling (–5 to –15°), to a suspension of 5.48 g (0.019 mole) of (IVa) in 70 ml of abs. 1,2-dimethoxyethane was added 1.92 g (0.02 mole) of t-BuONa. The stirring was continued for 2 h at 20°, the precipitate was filtered, and the filtrate was evaporated in vacuo. The residue was washed with abs. ether and then recrystallized from i-PrOH to give 3.1 g of unreacted (IIa) with mp 81° (decompn.). The ether solution was evaporated in vacuo, and the residue was distilled to give 1.21 g [89.0%, when based on reacted (IVa)] of (Ia) with bp 64-65° (0.6 mm).

Reaction of (IIa) with Dimethylamine. With stirring and cooling (–10 to –15°), to a solution of 2.25 g (0.05 mole) of Me_2NH in 40 ml of abs. MeCN was added in drops a solution of 5.72 g (0.02 mole) of (IIa) in 40 ml of abs. MeCN. The stirring was continued for 1 h at –10°, and another 2 h at 20°. The MeCN was evaporated in vacuo and the product was extracted from the residue with abs. ether. Removal of the ether and vacuum distillation of the residue gave 3.25 g (95.7%) of (Ia) with bp 64-65° (0.6 mm).

Reaction of (IIa) with Methylmagnesium Iodide. With stirring and cooling (–30 to –35°), to a solution of MeMgI from 7.1 g (0.05 mole) of MeI and 1.22 g (0.05 mole) of Mg in 60 ml of abs. ether, was added in an argon atmosphere 5.72 g (0.02 mole) of (IIa) in small portions. The stirring was continued for 5 h at 20° and the mixture was let stand overnight. The excess MeMgI was decomposed by adding 10 ml of satd. aqueous NH_4Cl solution, the ether layer was decanted and dried over $MgSO_4$, and the ether was removed in vacuo. Vacuum distillation of the residue gave 0.32 g (9.4%) of (Ia) with bp 64-65° (0.6 mm).

Model Reaction of (Ia) with Methylamine. A solution of 0.51 g (0.003 mole) of (Ia) in 3.50 g of $MeNH_2$ was kept in a sealed ampul for 3 h at 20°. The ampul was opened and let stand overnight to remove the $MeNH_2$. Based on the PMR spectral data, the residue (0.5 g) is pure nitrosamine (Ia).

Model Reaction of (Ia) with Dimethyl Sodiomalonate. A solution of 1.70 g (0.01 mole) of (Ia) and 1.54 g (0.01 mole) of dimethyl sodiomalonate in 60 ml of abs. MeCN was kept for 12 h at 20°. After removal of the MeCN in vacuo the products were extracted from the residue with abs. ether. The ether was removed in vacuo, while the residue (1.43 g), based on the PMR spectral data, is pure nitrosamine (Ia).

CONCLUSIONS

1. Some N,N-di-tert-alkyl-N'-alkoxydiazenium salts were synthesized by the O-alkylation of the corresponding nitrosamines.

2. It was shown that the N—Cl bond in 1-ethoxyimino-2,2,6,6-tetramethylpiperidinium chloride has an ionic character.

3. On the example of the reaction of 1-ethoxyimino-2,2,6,6-tetramethylpiperidinium tetrafluoborate with methylamine and sodiomalonic ester it was shown that N,N-di-tert-alkyl-N'-alkoxydiazenium salts are capable of aminoaminating nucleophiles.

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