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Heterocyclization of amino alcohols into saturated cyclic quaternary ammonium salts

Dmitry B. Vinogradov,* Pavel V. Bulatov, Evgeny Yu. Petrov and Vladimir A. Tartakovsky

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: lab42@mail.ru

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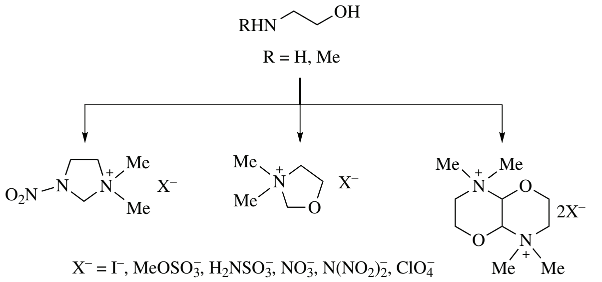
Cyclodehydration of available *N*-alkylethanolamines with aldehydes and simultaneous or subsequent quaternization afford functionalized quaternary ammonium salts of *N*-nitroimidazolidine, oxazolidine and annulated bis-morpholine type. Further replacement of their anions with residues of explosive acids provides a series of energy-intensive quaternary salts with a rich hydrogen content possessing satisfactory energy characteristics and sufficiently high thermal stability.



$X^- = I^-$, $MeOSO_3^-$, $H_2NSO_3^-$, NO_3^-, $N(NO_2)_2^-$, ClO_4^-

Keywords: ammonium quaternary salts, amino alcohols, nitrates, nitramines, aldehydes, heterocyclization.

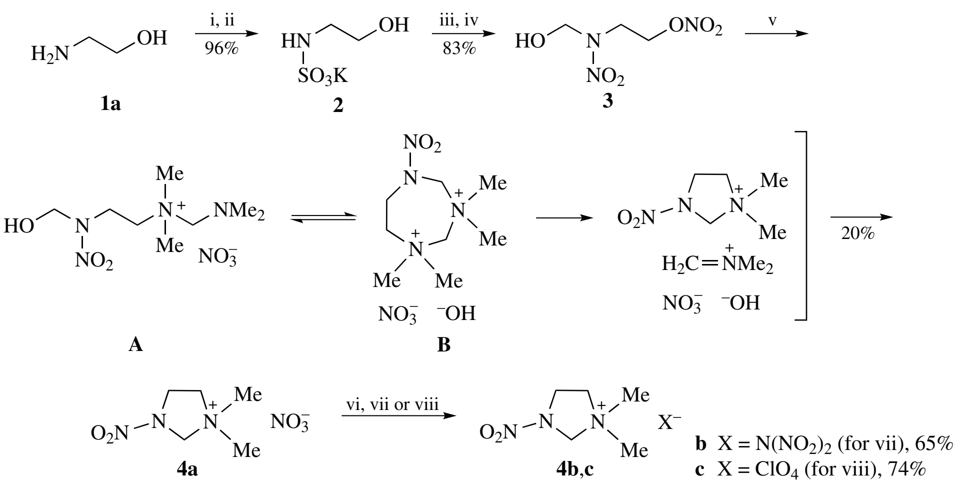
Recently, attention has been paid to quaternary ammonium salts with explosophore anions serving as fillers and/or combustion modifiers in solid rocket fuels and energy-rich basis for liquid water-based monofuels. This approach is interesting because the synthesis can involve selecting cation–anion pairs, which would provide the optimal set of properties for a specific task.[1–5]

Dinitramide salts are most stable in combinations with tertiary and quaternary alkylammonium cations.[6,7] For example, crystalline tetramethylammonium dinitramide melts with decomposition at 228 °C. This compound is soluble in water and water–alcohol solutions and is hydrolytically stable. Gafarov[8] reported a number of analogous salts and bis-azido-substituted trimethylammonium bases as examples of functionalized quaternary ammonium compounds. Earlier, Olah[9] described quaternary hydrazinium nitrates while Klapötke[10] prepared hydrazoic and other explosophore acid salts with polymethylated hydrazines. It was noted that crystalline salts were more stable than liquid or low-melting ones, and also the presence of a quaternary ammonium fragment dramatically increased the heat resistance and reduced sensitivity to shock and friction. Shreeve[11] reported a synthesis of energy-rich ionic liquids containing *N*-(2-azidoethyl)-*N*,*N*,*N*-trimethylammonium and *N*,*N*-bis(2-azidoethyl)-*N*,*N*-dimethylammonium salts with nitrocyanamide, dinitramide, dicyanamide and azide anions. The specific densities of these salts were within 1.15–1.41 g cm^{-3}, while their thermal decomposition temperatures were within 180–245 °C.

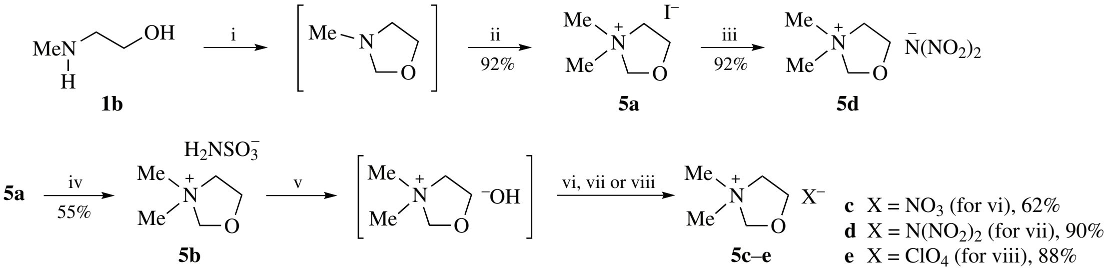
This work is a continuation of systematic studies[12] on the synthesis of energy-rich functionalized quaternary ammonium and hydrazinium salts. Previously, we dealt mostly with salts containing cations of linear structure. Here we propose the synthesis of quaternary salts of cyclic structure. In addition, we aimed at a qualitative assessment of the effect of their cyclic nature on the primary set of physicochemical properties, in particular, melting points and decomposition onset temperatures. We chose herein industrially available ethanolamine **1a** and *N*-methylethanolamine **1b** as the promising raw compounds.

It is known that sulfamate group can be easily converted to the nitramine one by treatment with nitrating agents. It was reported[13] that *N*-(2-hydroxyethyl)sulfamates of type **2** (K, Na, NH_4, Scheme 1) could be synthesized from ethanolamine **1a** by sulfonation with a pyridine–sulfotrioxide complex, however that method was expensive and required large amounts of solvents. In this work, potassium *N*-(2-hydroxyethyl)sulfamate **2** was obtained in a more rational way. As shown in Scheme 1, sulfamic acid was dissolved in a threefold excess of ethanolamine **1a** followed by keeping the resulting solution at an elevated temperature for a few hours and treatment with an ethanolic solution of potassium hydroxide. The resulting potassium ethanolsulfamate **2** was reacted with paraformaldehyde in glacial acetic acid followed by nitration with HNO_3/H_2SO_4 mixture to give *N*-[(2-nitroxyethyl)nitramino]methanol **3** (87%) with 13% admixture of ethylene dinitrate. This crude mixture was treated with *N*,*N*,*N'*,*N'*-tetramethyldiaminomethane in acetonitrile to afford colorless crystalline 3-nitro-1,1-dimethylimidazolidin-1-ium **4a** nitrate precipitated from the reaction mixture in 20% yield. This transformation seems to proceed first through the formation of a linear quaternary salt **A** (see Scheme 1) followed by intramolecular quaternization into seven-membered dication **B**. Unstable intermediate **B** would decompose into 3-nitro-1,1-dimethylimidazolidin-1-ium and dimethyl(methylidene)ammonium cations, which was fixed in mother liquor. Finally, nitrate **4a** precipitates to achieve equilibrium ratios in the mother liquor, which explains its low yield. A similar mechanism for reaction with *N*,*N*,*N'*,*N'*-tetramethyldiaminomethane was documented.[14] Further, nitrate **4a** was first converted to the base form in the aqueous solution by treatment with Dowex 2×8 anionite (OH^-) and then neutralized with ammonium salt of dinitramide or perchloric acid in the same solution to give salts **4b**,**c**, respectively (see Scheme 1).

The synthesis of 3,3-dimethyloxazolidin-3-ium iodide **5a** by quaternization of 3-methyloxazolidine with methyl iodide in 95% yield was reported previously.[15] The starting 3-methyloxazolidine was obtained in ~40% yield by the solvent-free

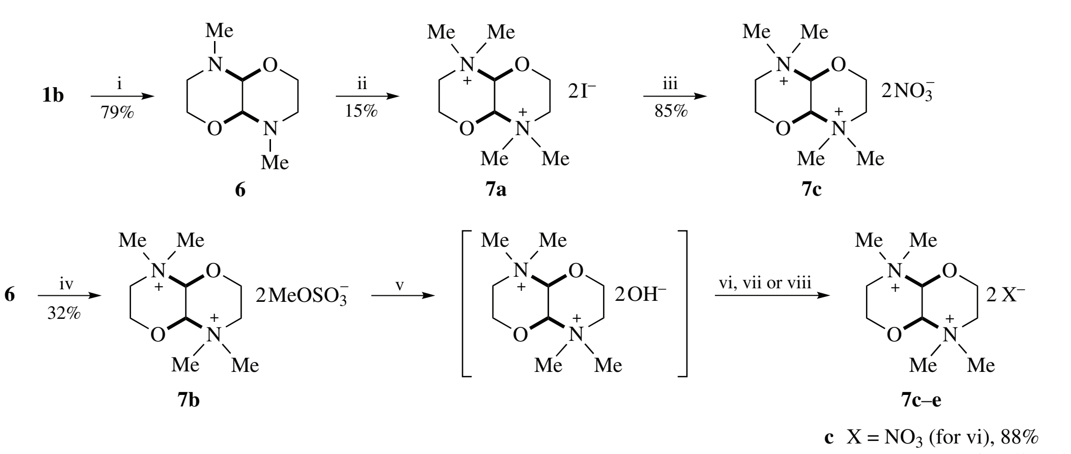


Scheme 1 *Reagents and conditions*: i, H_2NSO_3H, 178 °C, 9 h; ii, KOH, EtOH, room temperature, 40 min; iii, $(CH_2O)_x$, AcOH, room temperature, 20 min; iv, HNO_3/H_2SO_4, –15 °C, 1 h; v, $CH_2(NMe_2)_2$, MeCN, 45 °C, 30 min; vi, Dowex 2×8 $(OH^-)/H_2O$, room temperature, 1.5 h; vii, $NH_4N(NO_2)_2$, H_2O, room temperature, 20 min; viii, NH_4ClO_4, H_2O, room temperature, 20 min.



Scheme 2 *Reagents and conditions*: i, $(CH_2O)_x$, 40 °C, 3 h; ii, MeI, MeCN, room temperature, 20 h; iii, $AgN(NO_2)_2$, H_2O, room temperature, 30 min; iv, $Pb(H_2NSO_3)_2$, H_2O, room temperature, 30 min; v, NaOH, EtOH, THF, 0 °C, 40 min; vi, NH_4NO_3, H_2O, room temperature, 20 min; vii, $NH_4N(NO_2)_2$, H_2O, room temperature, 20 min; viii, NH_4ClO_4, H_2O, room temperature, 20 min.

reaction of *N*-methylethanolamine **1b** with paraformaldehyde in the presence of potassium carbonate followed by distillation.[16,17] We simplified the procedure by abandoning K_2CO_3 and performing both stages (Scheme 2) in one pot to obtain iodide **5a** in 92% total yield. The method of replacing the salt anion in an ion-exchange resin (*cf.* Scheme 1) did not give good results due to high solubility of 3,3-dimethyloxazolidin-3-ium salts in water. Therefore, iodide **5a** was converted to sulfamate **5b** by the reaction with aqueous lead sulfamate (see Scheme 2, conditions iv). A similar reaction of lead nitrate with iodide **5a** afforded 3,3-dimethyloxazolidin-3-ium nitrate **5c**, however, the thus obtained salt was not pure due to contamination with inorganic salts. In the meantime, a similar reaction of iodide **5a** with aqueous silver dinitramide provided the required 3,3-dimethyloxazolidin-3-ium dinitramide **5d** in high yield (conditions iii). To obtain similar salt with other anions, we employed a scheme involving the conversion of sulfamate **5b** to the base form in EtOH/THF medium and deposition of inorganic sulfamate, followed by ‘one pot’ reactions with ammonium nitrate, dinitramide or perchlorate. This approach gave the desired salts **5c–e** in high yields (see Scheme 2, conditions v–viii). Compound **5c** is a viscous oil, other salts are pale yellow (**5d**) or colorless (**5e**) crystalline substances.



Scheme 3 *Reagents and conditions*: i, $(CHOCHO)_3 \cdot 2H_2O$, 40 °C, 3 h; ii, MeI, MeOH, 40 °C, 10 h; iii, $Pb(NO_3)_2$, H_2O, room temperature, 30 min; iv, $(MeO)_2SO_2$, MeCN, 80 °C, 4 h; v, NaOH, EtOH, H_2O, THF, –10 °C, 30 min; vi, NH_4NO_3, H_2O, room temperature, 20 min; vii, $NH_4N(NO_2)_2$, H_2O, room temperature, 20 min; viii, NH_4ClO_4, H_2O, room temperature, 20 min.

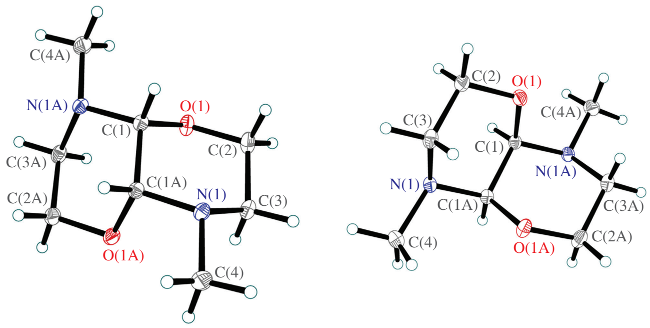


Figure 1 Molecular structure of isomeric (4a*R**,8a*R**)-4,8-dimethylperhydro[1,4]oxazino[3,2-*b*][1,4]oxazine **6**.

Though compounds **5c**,**d** showed rather high thermal stability, they had relatively low melting points. We assumed that their annulated dimerized analogues would have higher melting points and, accordingly, higher heat resistance. A synthesis of 4,8-dimethylperhydro[1,4]oxazino[3,2-*b*][1,4]oxazine **6** (annulated bis-*N*-methylmorpholine) was reported.[17] A procedure of quaternization of *N*-methyloxazolidine analogue[15] was tested herein toward diamine **6** (Scheme 3). However, this quaternization with iodomethane proceeded slowly due to the steric hindrance even at elevated temperatures. The yields of 4,4,8,8-tetramethylperhydro[1,4]oxazino[3,2-*b*][1,4]oxazine-4,8-diinium salts **7a**,**b** were also as moderate as 15–32% (see Scheme 3). According to X-ray crystallographic data, bicyclic compound **6** has a *cis*-junction (4a*R**,8a*R** relative configuration) of two 6-membered rings (Figure 1).† Obviously, the quaternary salts **7** formed from diamine **6** retain this spatial arrangement.

The reaction of diiodide **7a** with aqueous lead nitrate gave dinitrate **7c** in a high yield (see Scheme 3, conditions iii). Due to high solubility of sodium iodide in alcohol, the technique of synthesizing the other representatives by treatment with sodium hydroxide followed by reactions with ammonium salts with other anions was not satisfactory, Therefore, a different version using bis(methoxysulfonate) **7b** as the starting compound to prepare salts **8c–e** in high yields was employed (see Scheme 3, conditions v–viii). The salts appeared as colorless (**7c**,**e**) or pale yellow (**7d**) crystals, had high melting points and melted with decomposition. Diperchlorate **7e** did not melt but decomposed at 280 °C with a flash.

The resulting quaternary salts **4**, **5**, **7** containing *N*-nitroimidazolidine, oxazolidine and annulated bismorpholine rings were thermally stable crystalline non-hygroscopic compounds (with the exception for **5b**) whose properties are given in Table 1. For comparison, the corresponding properties of tetramethylammonium nitrate, dinitramide and perchlorate are also included.

One can see from the data in Table 1 that the resulting target nitrates, dinitramides and perchlorates of the corresponding cyclic quaternary ammonium bases **4**, **5**, **7** have a more rich oxygen balance (OB) and formation enthalpies in comparison with the starting tetramethylammonium salts, but nevertheless retain a sufficiently high hydrogen content and high heat resistance.

In conclusion, we rationally synthesized a number of quaternary salts of the *N*-nitroimidazolidine, oxazolidine and annulated bismorpholine type with nitrate perchlorate and dinitramide anions, and determined their melting points and decomposition onset. These compounds combine a rich hydrogen content with a sufficient oxygen balance and a satisfactory (in the case of dinitramides) heat of formation, they are stable in condensed state as well as in aqueous, water–alcohol and water–acetonitrile solutions without showing any noticeable hygroscopic properties. The resulting compounds are generally stable up to 190 °C or above. The physicochemical properties of these compounds may promote their use as high-hydrogen components of various propellant formulations. In addition, the good solubility of these salts in water or in a water/alcohol system, combined with their hydrolytic stability, makes it possible to use them as the main energy carrier in liquid water-based monofuel propellant systems.

Table 1 The properties of functionalized salts of quaternary ammonium bases.

Cation/compound	Anion	Mp/°C[a]	*T* (decomp.)/°C[a]	$\Delta H_{\mathrm{f(s)}}$ (calc.)/kcal mol^{-1}	H (%)	OB (%)[d]
Me$_4$N	NO$_3^-$	410[b]	410[b]	–78	8.88	–129.3
Me$_4$N	N(NO$_2$)$_2^-$	228	228	–24.5	6.71	–88.8
Me$_4$N	ClO$_4^-$	300	300	–62	6.97	–92.2
4a	NO$_3^-$	198–199	199	–47	5.81	–84.6
4b	N(NO$_2$)$_2^-$	82–83	190	+7	4.80	–63.5
4c	ClO$_4^-$	215–216	216	–30	4.92	–65.1
5a	I$^-$	184–185[c]	205			
5b	H$_2$NSO$_3^-$	hygroscopic				
5c	NO$_3^-$	oil	230	–77	7.37	–117.0
5d	N(NO$_2$)$_2^-$	83–84	170	–23	5.81	–84.6
5e	ClO$_4^-$	without melting	270–278	–60	6.00	–87.3
7a	I$^-$	209–210	210			
7b	(MeO)SO$_3^-$	without melting	>280			
7c	NO$_3^-$	245–246	246	–130	6.80	–112.8
7d	N(NO$_2$)$_2^-$	208–209	209	–23	5.35	–81.1
7e	ClO$_4^-$	without melting	280 self-ignition	–97	5.53	–83.8

[a] Stuart SMP-10 instrument (2 °C min^{-1}); [b] ref. 19; [c] 189 °C (ref. 15); [d] oxygen balance based on CO$_2$, for a compound C$_a$H$_b$N$_c$O$_d$, OB (%) = = 1600(d – 2a – b/2)/MW, MW is molecular weight.

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† *Crystal data for* **6**. Crystals of compound **6** suitable for the X-ray analysis were obtained by recrystallization from light petroleum. $C_8H_{16}N_2O_2$, orthorhombic, space group *Pbcn*, a = 14.2653(3), b = 4.66150(10) and c = 13.1875(3) Å, α = 90°, β = 90°, γ = 90°, V = 876.94(3) Å^3, Z = 4, d_{calc} = 1.304 g cm^{-3}, μ = 0.094 mm^{-1}, $F(000)$ = 376. Total of 37616 reflections were collected (2348 independent reflections, R_{int} = 0.0274) and used in refinement, which converted to wR_2 = 0.0878, GOF = 1.085 for all independent reflections [R_1 = 0.0308 was calculated for 2100 reflections with $I > 2\sigma(I)$].

CCDC 2015569 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2020.11.031.

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