Thermal decomposition of quaternary oxazolidinium bases

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Thermal decomposition of the quaternary oxazolidinium bases is accompanied by the nucleophilic attack of the hydroxyl group at the C(2) carbon atom of the cycle to afford carbonyl compounds and aminoalcohols.

Key words: quaternary oxazolidinium bases, ring-opening, redox reactions, 1-(2-dimethylaminoethoxy)alkenes, 10-methyl-7,13-dioxa-10-azaspiro[5.7]tridecane, 1-methyl-4,5,6,7-tetrahydroindole.

Decomposition of quaternary oxazolidinium bases of 1,2-aminoalcohols and their cyclic derivatives, morpholines, has been studied rather thoroughly.[1—3] However, thermal transformations of the quaternary bases and salts of such widespread cyclic derivatives of 1,2-aminoalcohols as oxazolidines remain practically unknown. There is some evidence that the reactions of dienophiles with 2-[*o*-(1-trimethylsilylalkyl)phenyl]-3,3-dimethyloxazolidinium iodides under the action of fluoride anion afford α-alkyl-α′-[2-(dimethylamino)alkoxy]-*o*-quinodimethanes as intermediates as a result of elimination of the trimethylsilyl group and oxazolidine ring opening.[4] The formation of *N*-methyl-*N*-(2-hydroxypropyl)-2-(cyclohexen-1-yloxy)ethylamine[5] and 8,10-dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane[6] in the reaction of 3-methyl-2,2-pentamethyleneoxazolidine with propylene oxide as a result of the cleavage of the quaternary oxazolidinium intermediate has also been reported.

The purpose of the present work was to study the main and side reactions that occur on thermal decomposition of quaternary oxazolidinium bases (QOB) and to elucidate the synthetic utility of this process. In this work we used a simplified procedure in which a mixture of the corresponding oxazolidinium iodide with an excess of NaOH rather than free QOB was subjected to decomposition.

Salts (**1a—e**) that contain substituents at the position 2 of the oxazolidine cycle with the α-H atoms gave the (2-aminoethoxy)alkenes (**3a—e**) (Scheme 1, Table 1).

According to the ^{1}H NMR data, the products of the decomposition of the QOB (**8**) (Scheme 2), *E*- and *Z*-enol ethers (**9A** and **9B**), are formed in a 2.2 : 1 ratio; enol ether (**9C**) is absent. This result is in accordance with the known concepts of decomposition of quaternary ammonium bases *via trans*-elimination proceeding by a E2 mechanism,[2] especially when it is considered that, for steric reasons, the antiperiplanar conformer (**8a**) appears to be preferable for the compound **8** than the synclinar one (**8b**).

The main competing reaction proceeding in the decomposition of the QOB is the nucleophilic substitution of the amino group at the C(2) atom of the cycle for a hydroxyl group to form carbonyl compounds (**5a—e**) and dimethylaminoethanol (**6**) (see Scheme 1). However, it should be noted that the content of **5a—e** and **6** in the reaction products does not allow one to estimate properly the extent of the competing reaction since these compounds undergo further transformations. For example, the decomposition of **2b** afforded, along with cyclohexanone (**5b**), 2-cyclohexylidenecyclohexanone and cyclohexanol (**15**) (Scheme 3), whose content was 23 % with respect to the amount of **5b**. The formation of **15** results from the known process of base-catalyzed reduction of carbonyl compounds with aminoalcohols.[7] For example, we have shown that **15** is formed on boiling of a mixture of **5b** with **6** and NaOH, and the final product of the oxidation of **6** is Me_2NH. The latter is also formed upon thermal decomposition of **2a—e** in a yield not greater than 1.5 %.

The decomposition of QOB (**10**), along with the expected ketone **5b**, alcohol **15**, and *N*-methyldiethanolamine, afforded 8,10-dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane (**12**) and 1-methyl-4,5,6,7-tetrahydroindole (**14**) (see Scheme 3). At the same time, we failed to isolate enol ether (**11**) due to the low concentration of this compound, although its formation is evidenced by the existence of the C=CH triplet (δ 4.58) in the ^{1}H NMR spectrum of the reaction mixture. The structure of **12** is proved by the absence of the absorption bands corresponding to stretching vibrations of the C=C, CH, and OH groups in its IR spectrum. ^{1}H and ^{13}C NMR spectra also unambiguously indicate the existence of the perhydro-1,3-dioxa-6-azocine structure.

The formation of **12** may result from the intramolecular nucleophilic substitution of the amino group at the C(2) atom of the oxazolidine cycle for the alkoxy anion in the intermediate (**10A**). A similar substitution at the α-C atom in the side chain of **10A** affords ethylene

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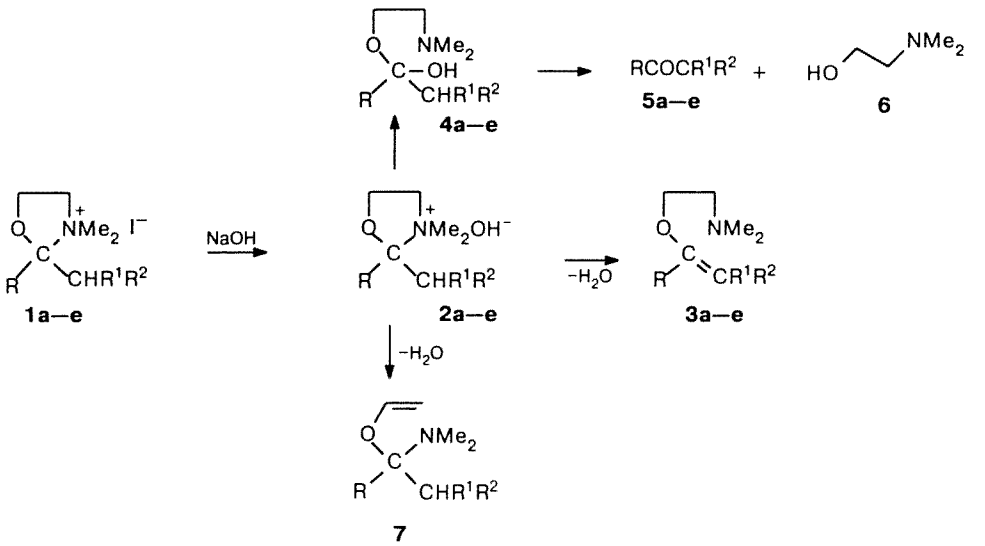
Scheme 1



R + R^1 = $(CH_2)_3$, R^2 = H (**a**); R + R^1 = $(CH_2)_4$, R^2 = H (**b**);
R + R^1 = $(CH_2)_5$, R^2 = H (**c**); R = H, R^1 = R^2 = Me (**d**);
R = Ph, R^1 = R^2 = H (**e**)

oxide and oxazolidine (**13**) that is typical of quaternary bases of 1,2-aminoalcohols.[1,2] According to the GLC analysis data, the amount of **13** in the reaction products does not exceed 0.5 %. This may be accounted for by the fact that, as we have shown before, **13** undergoes reductive-oxidative disproportionation under the action of NaOH to give indole **14**, alcohol **15**, and *N*-methylaminoethanol.[8]

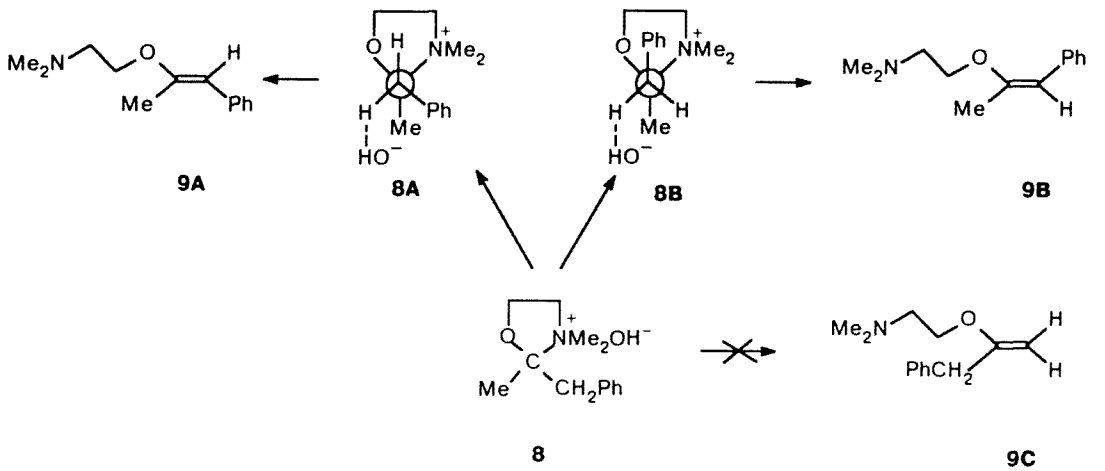
We expected that the decomposition of **2a—c** and **8** would also give vinyl ethers of the **7** type due to the

Table 1. Yields and characteristics of compounds **3a—e**, **9A**, **9B**, **12**, and **14**

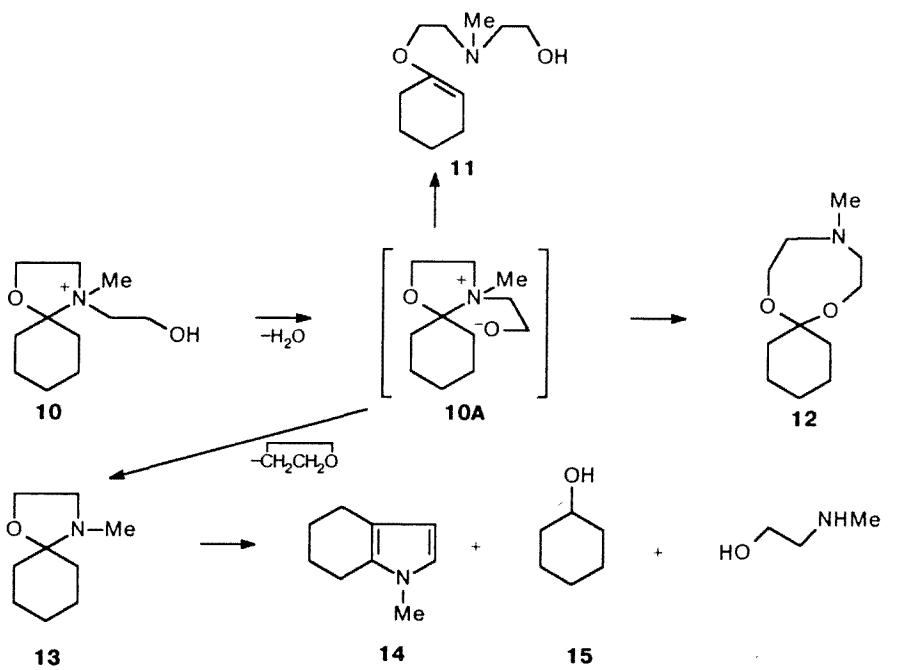
Compound	Yield (%)	B.p./°C (*p*/Torr)	n_D^{20}	d_4^{20}	Found / Calculated (%) C	H	N	Molecular formula
3a	24	83—87 (20)	1.4615	0.9269	69.26 69.63	11.24 11.04	9.15 9.02	$C_9H_{17}NO$
3b	41	108—110 (18)	1.4742	0.9265	70.84 70.96	11.53 11.31	8.14 8.27	$C_{10}H_{19}NO$
3c	36	118—120 (18)	1.4782	0.9288	71.94 72.08	11.60 11.55	7.82 7.64	$C_{11}H_{21}NO$
3d	23	143—147 (727)	1.4370	0.8472	66.78 67.09	11.95 11.96	9.66 9.78	$C_8H_{17}NO$
3e	32	139—140 (12)	1.5248	0.9794	75.09 75.35	9.03 8.96	7.46 7.32	$C_{12}H_{17}NO$
9A,B[a]	40	150—152 (18)	1.5314	0.9691	76.04 76.06	9.24 9.32	6.43 6.82	$C_{13}H_{19}NO$
12	3	105—108 (8)	1.4838	1.0314	66.01 66.30	10.34 10.62	6.94 7.03	$C_{11}H_{21}NO_2$
14[b]	12	91—94 (8)	1.5282	0.9901				

[a] The data for the mixture of **9A** and **9B** isomers in a 2.1 : 1 ratio are given. [b] Literature data:[7] b.p. 103—104 °C (11 Torr), n_D^{20} 1.5287, d_4^{20} 0.9906.

Scheme 2



Scheme 3



elimination of the H atom at the C(5) atom of the cycle. However, judging from the ^{1}H NMR spectra of the reaction mixtures, the ethers **7** are in no case formed or they are decomposed (hydrolyzed) under the drastic reaction conditions. Owing partly to this process, ketones **5a—e** and Me_2NH may be formed.

An attempt to synthesize a vinyl ether of the **7** type from oxazolidinium salt (**16**), which does not contain the α-H atoms in the substituent at the C(2) atom of the cycle, afforded a multicomponent mixture of the reaction products (14 compounds according to GLC); compounds with a vinyloxy group were also not found among the products (according to the ^{1}H NMR data).

Methanol, aminoalcohol **6**, benzaldehyde, benzyl alcohol (**17**), 2-phenyldioxolane (**18**), and 3-methyl-2-phenyloxazolidine (**19**) were identified in this mixture by GLC; their concentrations were 2, 45, 0.5, 10, 0.2, and 3 %, respectively (Scheme 4). Only alcohols **6** and **17** were isolated in 38 and 7 % yields. In addition, benzoic acid was isolated in 19 % yield from the alkaline bottoms after pyrolysis. Such composition of the reaction products indicates that the main processes, proceeding also in this case, are the substitutions at α-C atoms (mainly, at the C(2) atom of the cycle). The benzaldehyde formed undergoes Cannizzaro redox disproportionation, which is proved by the isolation of benzoic acid.

Scheme 4

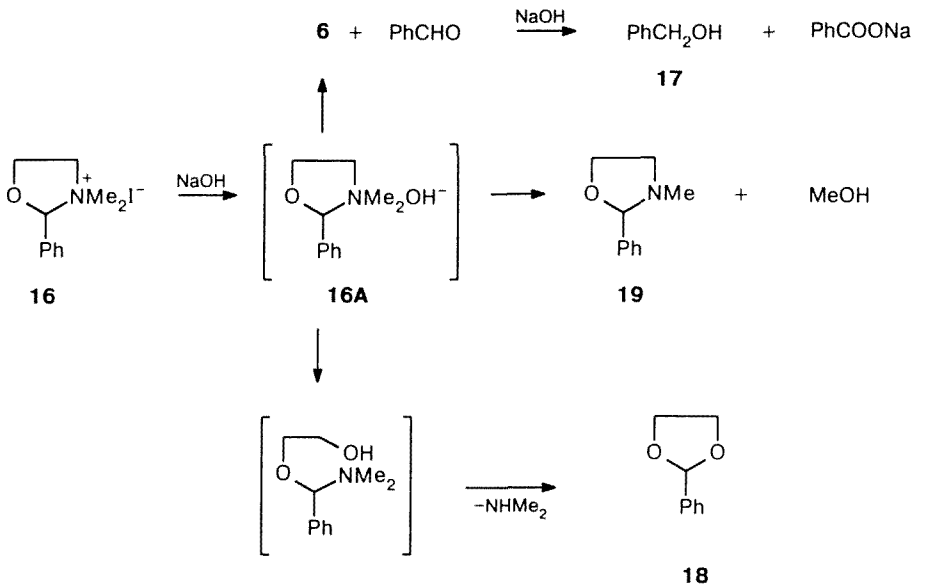


Table 2. IR and NMR spectral data for compounds **3a—e**, **9A**, **9B**, and **12**

Compound	IR, ν/cm^{-1}	^{1}H NMR ($CDCl_3$), δ (J/Hz)
3a	1635 (C=C); 3070 (=C—H)	1.65—2.20 [m, 6 H, $(CH_2)_3$]; 2.27 (s, 6 H, NMe_2); 2.60 (t, 2 H, NCH_2); 3.81 (t, 2 H, OCH_2); 4.43 (t, 1 H, C=CH)
3b	1645 (C=C); 3040 (=C—H)	1.58 (m, 4 H, $(CH_2)_2$); 2.03 (m, 4 H, $CH_2C{=}CCH_2$); 2.26 (s, 6 H, NMe_2); 2.58 (t, 2 H, NCH_2); 3.71 (t, 2 H, OCH_2); 4.59 (t, 1 H, C=CH)
3c	1645 (C=C); 3055 (=C—H)	1.57 [m, 6 H, $(CH_2)_3$]; 2.04 (m, 4 H, $CH_2C{=}CCH_2$); 2.26 (s, 6 H, NMe_2); 2.57 (t, 2 H, NCH_2); 3.62 (t, 2 H, OCH_2); 4.69 (t, 1 H, C=CH)
3d	1675 (C=C); 3070 (=C—H)	1.52 (d, 3 H, MeC=CO-*trans*, ^4J = 1.46); 1.59 (d, 3 H, MeC=CO-*cis*, ^4J = 1.46); 2.27 (s, 6 H, NMe_2); 2.52 (t, 2 H, NCH_2); 3.74 (t, 2 H, OCH_2); 5.77 (m, 1 H, C=CH, ^4J = 1.46)
3e	1570, 1595, 1635 (C=C); 3030, 3050, 3070 (=C—H)	2.27 (s, 6 H, NMe_2); 2.70 (t, 2 H, NCH_2); 3.96 (t, 2 H, OCH_2); 4.16 (d, 1 H, OC=CH-*trans*, ^2J = 2.5); 4.57 (d, 1 H, OC=CH-*cis*); 7.26—7.56 (m, 5 H, Ph)
9A,B[a]	1575, 1590, 1635 (C=C); 3035, 3045, 3070 (=C—H)	1.98 [s, 2.04 H, C=CMe (**A**)]; 2.01 [s, 0.96 H, C=CMe (**B**)]; 2.28 (s, 6 H, NMe_2); 2.63 (m, 2 H, NCH_2); 3.90 (m, 2 H, OCH_2); 5.30 [s, 0.32 H, C=CH (**A**)]; 5.57 [s, 0.68 H, C=CH (**B**)]; 7.21—7.55 (m, 5 H, Ph)
12[b]	935, 1020, 1065, 1095, 1135, 1260, 1325, 1350, 1430, 2780, 2840, 2920	1.52 [m, 10 H, $(CH_2)_5$]; 2.44 (s, 3 H, Me); 2.68 (t, 4 H, CH_2NCH_2); 3.72 (t, 4 H, CH_2OCH_2)

[a] The IR and ^{1}H NMR spectra for a mixture of **9A** and **9B** isomers. [b] ^{13}C NMR ($CDCl_3$), δ: 22.34 (C(2) and C(4)); 24.95 C(3)); 33.08 C(1)) and C(5)); 45.05 (N—Me); 57.20 (CN_2N); 59.63 (CH_2O); 99.67 (OCO). MS (EI, 70 eV), m/z (I_{rel}(%)): 199 $[M]^+$ (11), 101 $[Me{-}OC(CH_2)_5]^+$ (19), 72 (10), 71 (67), 70 (12), 58 (52), 57 (9), 55 (11), 44 (12), 43 (100).

Thus, the thermal decomposition of quaternary oxazolidine bases may be of interest for the preparative synthesis of enol ethers. The low yield of the latter (1.5—2 times lower than in the case of the decomposition of quaternary morpholinium bases)[2,3] is compensated by the simplicity of the synthesis and accessibility of the starting oxazolidines.[9]

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Jeol FX-90Q instrument (90 and 22.49 MHz) with HMDS as the internal standard. IR spectra were obtained on a Specord 75-IR spectrophotometer in thin layers. Mass spectra were recorded on a Varian MAT-212 chromato mass-spectrometer.

The control of purity and the identification of compounds in the reaction mixtures were carried out by GLC on a LKhM-80 chromatograph using a katharometer as the detector, helium as the carrier gas, and a steel column (3000×3 mm) with 3 % OV-17 on Inerton super (0.160—0.200 mm); the temperature was programmed from 50 to 250 °C at the rate of 4 deg min^{-1}.

Thermal decomposition of oxazolidine bases. General procedure. A mixture of an oxazolidinium salt (0.5 mol) and finely ground NaOH (2 mol) was heated in a steel flask until the distillation ceased. The condensate collected was dried with K_2CO_3 and its qualitative and quantitative composition were determined by GLC and ^1H NMR. Individual products were then isolated by rectification on a column (10 t.p.)

In the case of oxazolidinium salt **16**, the solid residue after the reaction was acidified with HCl and extracted with ether (3×50 mL) to give 0.048 moles of benzoic acid.

The yields and characteristics of the compounds obtained are given in Table 1 and the IR and NMR spectral data are given in Table 2.

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