2. Structure of a boron-free hydrolysis product from Boromycin

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Summary. The structure of *des*-boron-*des*-valine-boromycin $C_{40}H_{68}O_{14} \cdot H_2O$ (DBDVB), the product obtained by hydrolysis of the antibiotic boromycin $C_{45}H_{74}BNO_{15}$, has been determined by X-ray analysis. The molecule is remarkably similar in constitution, configuration and even in conformation to those of boromycin and *des*-valine-boromycin determined previously [2], showing that the overall molecular shape is retained on removal of the spiro boron atom.

Boromycin $C_{45}H_{74}BNO_{15}$ is a boron-containing antibiotic produced by certain strains of *Streptomyces antibioticus* [1]. It has been shown by a combination of chemical evidence with X-ray analysis that the molecule is a D-valine ester of a *Böeseken*-complex of boric acid with a macrodiolide of a new type [2]. The X-ray analysis was actually carried out not on boromycin itself but on Cs and Rb salts of *des*-valine-boromycin (DVB for short), a product obtained by mild alkaline hydrolytic cleavage of D-valine. By mild acid hydrolysis DVB splits off boric acid, yielding a polyhydroxy product that we refer to as *des*-boron-*des*-valine-boromycin (DBDVB). Since various attempts to reconstitute the *Böeseken*-complex were unsuccessful, it seemed possible that the acid hydrolysis was accompanied by changes in constitution and/or configuration. In boromycin and DVB the boron atom forms a spiro junction between two five-membered rings attached to opposite sides of the macrocycle. This spiro junction could be assumed to contribute significantly to the overall conformational rigidity of the macrocycle and its removal might lead to a much more flexible molecule in which many intramolecular reactions between numerous functional groups under acidic conditions can be imagined.

We have now determined the structure of DBDVB by X-ray analysis. Unexpectedly, perhaps, the molecule turns out to be the unrearranged hydrolysis product **1** formally derivable from DVB by removal of B^- and addition of four hydrogen atoms to give four extra hydroxyl groups. The configurations at all 15 asymmetric carbon atoms are the same as in DVB [2][3]) and the conformation is also remarkably similar to that of DVB in spite of the removal of the spiro junction.

DBDVB crystallizes from ethyl acetate solution as a monohydrate ($C_{40}H_{68}O_{14} \cdot H_2O$) with 4 formula units in an orthorhombic unit cell of dimensions a = 12.857, b = 29.878, c = 11.347 Å, space group $P2_12_12_1$. The structure was solved by application of phase relationships and has been refined by least-squares analysis to a conventional R-factor of 0.09, based on approximately 2240 observed structure amplitudes.

Positional coordinates of all carbon and oxygen atoms are listed in Table 1. The estimated standard deviations in position lie in the ranges 0.007–0.012 Å for O and

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[3]) In the structure shown for boromycin and *des*-valine-boromycin [2] the chirality descriptors for atoms 2 and 2′ should be changed from *R* to *S*.

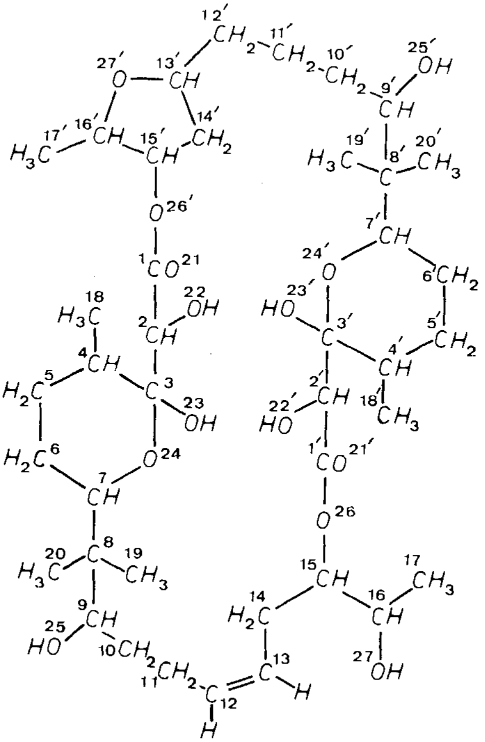
0.010–0.016 Å for C, corresponding to standard deviations in interatomic distances in the range 0.01 Å (for the best O··O distances) to 0.025 Å (for the worst C–C distances). Anisotropic temperature factors and hydrogen positions are not listed here,

Table 1. *Final Positional Parameters* (× 10^4) *and Vibration Parameters* (U(ij) × 10^2))

Atom	*x*	*y*	*z*	U(11)	U(22)	U(33)	U(12)	U(13)	U(23)
C(1')	3583(10)	0974(4)	2126(12)	5.12	4.91	7.44	-0.11	0.67	1.78
C(2')	3976(9)	1045(4)	3350(10)	4.26	5.86	4.16	0.99	0.25	-0.20
C(3')	4181(9)	0598(4)	4031(10)	4.89	5.28	4.71	0.67	1.37	-0.30
C(4')	3139(9)	0366(4)	4374(11)	3.29	7.19	5.84	-0.20	-0.19	0.40
C(5')	3382(10)	-0103(4)	4857(12)	5.06	7.77	8.71	-1.24	0.58	2.16
C(6')	4030(10)	-0383(4)	3973(13)	6.08	6.35	9.55	-0.41	1.98	1.69
C(7')	4998(9)	-0129(4)	3681(10)	5.04	4.54	5.80	-0.54	0.70	1.00
C(8')	5750(10)	-0356(4)	2773(11)	7.01	4.24	5.20	0.70	-0.23	0.59
C(9')	6636(8)	-0022(4)	2526(10)	2.58	5.42	5.79	0.28	1.00	0.80
C(10')	7604(10)	-0235(4)	1950(11)	5.56	6.70	6.28	0.25	0.95	-0.20
C(11')	8481(10)	0111(4)	1625(12)	6.41	7.21	6.97	0.45	1.63	-0.43
C(12')	8871(9)	0388(4)	2681(11)	4.28	6.09	6.29	1.57	1.61	2.01
C(13')	9730(10)	0699(4)	2317(11)	5.48	7.21	6.25	1.19	3.19	1.34
C(14')	0167(9)	0983(4)	3324(12)	3.24	8.11	7.85	-0.02	2.08	-0.47
C(15')	9726(9)	1433(4)	3109(12)	4.14	7.98	6.43	-1.07	2.33	0.15
C(16')	9508(8)	1456(4)	1799(11)	2.44	6.49	6.78	-0.42	1.13	-0.21
C(17')	0459(12)	1631(5)	1148(13)	9.42	11.60	7.89	-2.76	2.16	1.55
C(18')	2522(10)	0639(5)	5295(12)	4.19	11.26	6.50	0.09	0.60	-1.28
C(19')	5179(10)	-0485(4)	1613(12)	5.49	8.74	7.07	0.88	-1.47	-2.08
C(20')	6217(10)	-0779(4)	3383(12)	6.41	6.28	7.35	0.89	1.03	1.00
O(21')	2665(6)	0897(3)	1906(8)	2.16	13.36	7.02	0.40	-0.39	0.38
O(22')	4897(6)	1309(3)	3352(8)	3.87	6.52	7.68	-0.42	-0.65	-0.44
O(23')	4775(6)	0685(3)	5026(6)	4.56	6.91	4.05	0.39	-1.11	-0.59
O(24')	4721(5)	0313(2)	3193(7)	3.31	4.72	5.37	0.70	-0.07	0.64
O(25')	6309(6)	0333(3)	1750(8)	4.52	5.84	7.44	0.58	1.22	2.00
O(26')	8650(5)	1425(3)	3659(7)	2.68	7.81	5.43	-0.24	0.29	-0.83
O(27')	9371(7)	1005(3)	1455(8)	8.60	7.63	7.41	-1.29	-0.58	1.30
C(1)	8592(10)	1508(4)	4810(11)	5.00	6.20	6.34	1.12	-0.38	0.49
C(2)	7406(9)	1437(4)	5267(11)	4.18	5.46	6.32	0.19	2.24	0.31
C(3)	6955(9)	1892(4)	5407(12)	3.72	6.43	7.33	-0.32	1.00	0.36
C(4)	7213(10)	2115(4)	6555(12)	6.34	8.69	6.40	1.54	0.58	-0.60
C(5)	6858(12)	2617(5)	6550(13)	9.06	9.09	7.29	0.72	-1.20	-2.80
C(6)	7215(11)	2864(4)	5445(14)	7.70	6.83	9.54	0.08	0.37	-1.76
C(7)	6886(10)	2611(4)	4355(12)	7.26	4.97	7.60	0.99	-0.19	-0.94
C(8)	7216(9)	2806(4)	3190(13)	5.55	4.63	9.83	-1.06	-0.04	-0.48
C(9)	6899(11)	2527(4)	2147(13)	8.35	4.38	9.32	-0.43	1.17	1.29
C(10)	5671(9)	2442(5)	2066(12)	4.48	8.34	8.23	0.81	-1.18	-0.03
C(11)	5391(11)	2265(4)	0867(13)	6.24	8.12	10.01	0.27	0.32	1.19
C(12)	4205(12)	2170(4)	0781(13)	8.67	7.82	9.27	2.74	-1.57	0.47
C(13)	3842(12)	1823(5)	0257(14)	8.58	8.95	9.87	-0.02	-0.64	1.07
C(14)	4338(10)	1449(4)	-0385(12)	6.74	6.50	6.71	0.80	-2.17	1.56
C(15)	4052(9)	1001(4)	0053(10)	3.59	6.95	4.41	0.37	0.05	1.16
C(16)	4486(9)	0606(4)	-0540(11)	4.46	9.78	4.84	0.82	-0.96	-2.16
C(17)	4225(11)	0595(5)	-1819(13)	6.50	13.34	7.48	2.14	-1.66	-0.87
C(18)	6813(14)	1879(5)	7661(13)	12.79	12.34	7.30	4.12	0.46	-0.25
C(19)	8459(12)	2825(5)	3148(15)	9.13	9.41	10.44	-3.57	0.59	2.01
C(20)	6824(12)	3286(4)	3069(15)	9.77	5.21	13.53	-1.90	2.09	0.92
O(21)	9297(6)	1623(3)	5442(8)	3.78	12.38	8.19	1.06	-0.31	-1.28
O(22)	6901(6)	1147(3)	4523(8)	4.05	6.46	8.85	-0.13	0.36	-1.34
O(23)	5818(6)	1837(3)	5400(8)	2.78	8.35	8.55	0.85	2.12	0.67
O(24)	7218(6)	2159(3)	4428(8)	4.03	5.13	9.23	0.06	0.52	1.45
O(25)	7414(7)	2106(3)	2066(8)	6.03	6.43	9.48	0.19	0.16	-0.50
O(26)	4321(6)	0983(3)	1311(7)	3.34	7.81	4.85	0.18	0.59	0.67
O(27)	5631(6)	0640(3)	-0528(8)	4.25	13.01	8.05	2.13	0.03	-0.41
O(55)	6662(6)	1246(3)	2058(9)	4.61	8.07	10.40	-0.57	-0.34	0.59

although in a final difference-synthesis well defined electron-density peaks for most of the 70 hydrogen atoms present were found in stereochemically reasonable positions. The hydrogen atoms of the seven hydroxyl groups and of the water molecule could not be located with confidence from the difference synthesis.

With one or two exceptions, bond distances and angles derived from the coordinates agree within experimental error with values expected for structure **1**. The worst agreement is for the bond C(1)–C(2) where the calculated distance 1.624 Å (e.s.d. 0.017 Å) is about 0.1 Å longer than a standard C(sp^2)–C(sp^3) distance; neither atom has an abnormally large or anisotropic thermal parameter. The chemically equivalent bond C(1′)–C(2′) in the other half of the molecule appears to be normal or even slightly short (1.493 Å). In view of this and other similar discrepancies, the analysis does not seem sufficiently accurate to justify any detailed discussion of the bond distances and angles. However, the constitution and configuration of the molecule can be regarded as established by the analysis. The absolute configuration follows from the earlier analysis of the Cs-salt of DVB [2].



One might have expected that the constraint due to the presence of the spiro boron junction in boromycin and in DVB is essential for maintaining the secondary structure of these molecules. This does not seem to be the case, for the conformation found in the crystal for the *des*-boron derivative is closely similar to that of DVB. This similarity can be inferred from Table 2, which lists the torsion angles round bonds in the main 28-membered ring of both molecules. A pictorial comparison is provided by Figure 1, which shows a perspective view of the main ring with its hydroxyl substituents for both molecules. It is clear that removal of the boron atom has led to only minimal conformational changes, apart from those associated with movement of the oxygen atoms O(22), O(22'), O(23) and O(23'), those directly bonded to boron in DVB. In particular, the oxygen-lined cleft that houses the counter-ion to the negatively charged boron atom in the *Böeseken* complexes is also present in the *des*-boron derivative, where it accomodates a water molecule.

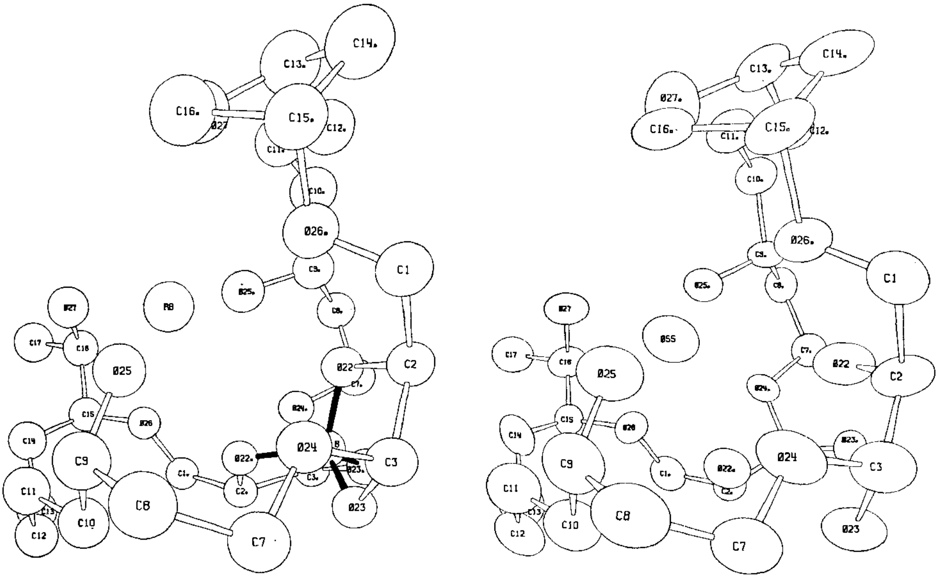


Fig. 1. *Perspective view of the main 28-membered ring in DVB* (Rb^+salt) *and DBDVB* (with attached water molecule O(55)). Oxygen substituents are shown but others have been omitted for the sake of clarity. The ellipsoids represent the appropriate projections of the vibration tensors given in Table 1.

A detailed comparison of the environments of Rb^+ in DVB and H_2O in DBDVB shows some interesting similarities. In DVB the Rb is surrounded by eight oxygen-atoms at distances of 2.80–3.17 Å (Table 3). The coordination polyhedron is irregular and does not even remotely resemble any of the standard types for 8-coordination –cube, square antiprism or rhombic dodecahedron. If the completely triangulated polyhedron is constructed, as can be done from the O···O distances given in Table 3, it is found to have the form shown in Figure 2 with six 5-connected vertices and two 3-connected ones. A complete list of the 257 non-isomorphous polyhedra with eight vertices has been tabulated recently [3], and the one shown in Figure 2 corresponds to No. 10 in the list. The two adjacent triangles formed by O(22), O(25'), O(26') and O(27') are actually coplanar to within 0.03 Å, and deletion of the common edge O(22)–O(27') to give a quadrilateral face would lead to polyhedron No. 47 in the list. All other pairs of adjacent triangles in Figure 2 are non-coplanar with r.m.s. deviations of at least 0.13 Å.

Table 2. *Comparison of Main Ring Torsion Angles in DVDBB and DVB*

Angle about bond	DVDBB	DVB
C(1′)—C(2′)	– 95.6	–105.1
C(2′)—C(3′)	44.6	41.1
C(3′)—O(24′)	179.3	172.5
O(24′)—C(7′)	–169.4	–167.7
C(7′)—C(8′)	52.6	56.7
C(8′)—C(9′)	162.9	161.5
C(9′)—C(10′)	176.3	174.1
C(10′)—C(11′)	57.3	64.1
C(11′)—C(12′)	178.0	–177.4
C(12′)—C(13′)	–179.5	179.1
C(13′)—C(14′)	–105.0	–104.7
C(14′)—C(15′)	83.9	78.3
C(15′)—O(26′)	83.9	77.0
O(26′)—C(1)	–174.5	–172.3
C(1)—C(2)	–103.0	– 99.5
C(2)—C(3)	44.3	37.1
C(3)—O(24)	–179.4	178.9
O(24)—C(7)	–176.4	–174.2
C(7)—C(8)	51.8	63.0
C(8)—C(9)	57.6	57.8
C(9)—C(10)	165.9	168.1
C(10)—C(11)	178.8	175.8
C(11)—C(12)	–139.5	–141.8
C(12)—C(13)	– 1.7	– 1.6
C(13)—C(14)	125.6	112.8
C(14)—C(15)	– 56.9	– 49.7
C(15)—O(26)	109.9	97.9
O(26)—C(1′)	–168.9	–167.3

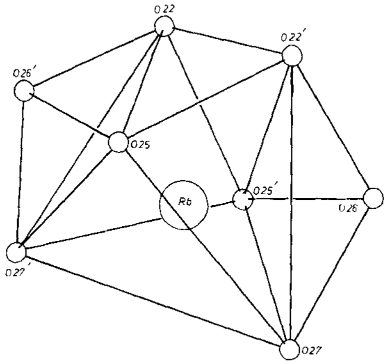


Fig. 2. *The completely triangulated coordination polyhedron of the Rb$^+$ cation in the DVB salt.* The corresponding polyhedron formed by the oxygen atoms surrounding the water molecule in DBDVB is very similar. In both polyhedra the quadrilateral O(22), O(25′), O(27′) and O(26′) is approximately coplanar.

The H_2O molecule in the *des*-boron derivative is also surrounded by eight oxygenatoms, at distances of 2.71–3.69 Å (Table 3). Although this range of distances is wider than in the previous case the same completely triangulated polyhedron (No. 10), somewhat elongated along the direction O(27)–O(27′), is obtained. Also the same four oxygen atoms lie in an approximately coplanar (to within 0.05 Å) quadrilateral face,

Table 3.

A. *Rb...O and H_2O...O Distances* (Å)

DVDBB		DVB	
O(55)....O(22)	2.83	Rb....O(22)	3.01
O(22′)	2.71	O(22′)	2.93
O(25)	2.75	O(25)	2.88
O(25′)	2.79	O(25′)	2.80
O(26)	3.22	O(26)	3.07
O(26′)	3.18	O(26′)	3.17
O(27)	3.69	O(27)	2.92
O(27′)	3.62	O(27′)	3.07

B. *O....O Distances* (Å) *in DVDBB and DVB*

		DVDBB							
		O(22)	O(25)	O(26)	O(27)	O(22′)	O(25′)	O(26′)	O(27′)
DVB	O(22)	–	4.05	4.95	6.15	2.94	4.05	2.59	4.73
	O(25)	3.86	–	5.27	5.75	4.28	5.50	3.15	4.20
	O(26)	4.45	4.83	–	2.87	2.62	3.25	6.32	6.50
	O(27)	5.67	5.03	2.81	–	4.93	2.88	6.57	5.42
	O(22′)	2.38	3.73	2.63	4.72	–	3.89	4.85	6.20
	O(25′)	3.67	5.58	3.28	3.50	3.78	–	4.94	4.43
	O(26′)	2.62	3.18	5.92	6.00	4.37	4.79	–	2.95
	O(27′)	4.49	4.28	6.03	4.86	5.68	4.34	2.76	–

Other short O...O Distances in DVDBB (Å)

O(25) ...O(24)	2.70	O(22) ...O(23)	2.68
O(25′)...O(24′)	2.62	O(22′)...O(23′)	2.67

and all other pairs of adjacent triangular faces are non-planar. Considering that there are 257 non-isomorphous polyhedra with eight vertices the fact that the same irregular one can be recognized in the boron-containing and the boron-free molecule is striking and unexpected.

It is clear that the arrangement of atoms forming the cleft is altered only very slightly on removal of the spiro boron junction and hence does not depend for its stability on the geometric constraints introduced by this junction. Furthermore, although hydrogen bonding presumably contributes somewhat to the stability of the cleft in both DVB and DBDVB it cannot be the determining factor since the bonding patterns must be very different in the two structures. The cleft can be regarded as an expression of the stable secondary structure of the 28-membered ring with its substituents, just as the clefts associated with the active sites of some enzymes are expressions of the secondary structure of a polypeptide chain with a particular sequence of side-chains.

In boromycin itself the negative charge of the spiro boron atom is neutralized by the $-NH_3^+$ group of the D-valine residue; as pointed out previously [2] this $-NH_3^+$ group can be and probably is accomodated in the cleft, which is thereby blocked by the lipophilic isopropyl side-chain of the amino acid. The biological relevance of this structural feature may become clear when the biochemical function of boromycin is better understood.

Experimental Part

Since the crystals deteriorate slowly in the atmosphere the specimen used for X-ray analysis was sealed in a borax-glass capillary. Intensities of 3840 independent reflections were measured with a 4-circle diffractometer, (*Hilger & Watts* Model Y290 under control of a PDP-8 computer) using MoKα radiation ($\lambda = 0.71069$ Å) monochromatized by reflection from graphite, and converted, after the usual corrections, to corresponding F-values (structure amplitudes) and E-values (normalized structure amplitudes).

The initial attempt to solve the phase problem was based on the 462 reflections with $E \geq 1.40$, using the multiple solution (MULTAN) technique [4]. After choosing three reflections to define the origin, sixteen ways of assigning phases to four reflections (one defining the enantiomorph) were tested. The one that produced the highest 'figure of merit' [4] and the lowest residual $((\Sigma|E_o\text{-}E_c|)/(\Sigma E_o))$ yielded an E-map in which a structurally reasonable fragment, consisting of a six-membered ring with two sidechains, could be recognized. However, subsequent tangent refinement on this fragment using MULTAN did not lead to any obvious improvement or recognizable enlargement of the fragment. This lack of success led us to consider the possibility that the orientation of the fragment in the unit cell might be correct but its position wrong. As *Karle* [5] has pointed out, the 'difference' synthesis with coefficients $(E_0^2\text{-}E_c^2)^2$ should, in such circumstances, contain peaks at positions corresponding to the vectors between the assumed position of the fragment and its correct position. We tried several assumed positions but had to conclude in the end that if the fragment was indeed present in the structure and correctly oriented its initial assumed position could not be improved on.

Re-examination of the original E-map revealed the presence of a second possible fragment of six atoms with reasonable interatomic distances and angles. A model consisting of both fragments (19 atoms) yielded an R-value of 0.48. When the corresponding F_o-synthesis was compared with the E-map, they showed 24 strong peaks common to both, which could be accepted as indicating provisional atomic positions. At the cost of three subsequent iterations of tangent refinement followed by F_o-syntheses it was only possible to increase the number of acceptable peaks to 26.

At this point further progress seemed likely only if a greater measure of external control could be exercised over the number of tangent refinement cycles calculated and the behaviour of phases of individual reflections from cycle to cycle. We therefore switched to a locally written program [6] which allowed this. Imput phases were restricted to reflections for which the ratio E_c/E_o was greater than 0.5. Starting with a set of 370 phases, chosen in this way, seven cycles of tangent refinement yielded stable phases for 451 reflections and a residual of 0.25. The resulting E-map revealed the positions of 45 out of the expected 54 heavy atoms. The remaining nine, as well as an additional peak ascribed to the O of a water molecule, were located from a subsequent $(F_o\text{-}F_c)$-synthesis.

After this the refinement followed a fairly straight forward course. Three cycles of full-matrix least-squares refinement with all atoms assigned isotropic temperature factors reduced the R-value from 0.26 to 0.15. Three additional cycles (anisotropic, block-diagonal) gave further reduction in R to 0.115. By this stage, the identification of the various atoms as C or O, based partly on the behaviour of the temperature factors and partly on analogy with the known structure of the B-containing compound, was complete. Hydrogen atoms (except those of hydroxyl groups) could therefore be placed at stereochemically reasonable positions and included in the structural model. Four final refinement cycles (H-atoms included but not refined) lowered the R-value to 0.09 for the reflections with $F_o > \sigma(F_o)$. Weights assigned throughout the least-squares analysis were inversely proportional to the variance in F_o as estimated from counting statistics. Final positional and thermal parameters are listed in Table 1.

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3. Thermochemical Kinetics of Nitrogen Compounds

Part 4

The Gas Phase Unimolecular Thermal Decomposition of Triallylamine[1]

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(3. IX. 73)

Summary. The gas phase thermal decomposition of triallylamine was studied in the temperature range 531 to 620 K. The major products observed in the reaction were propylene and 3-picoline. The first order rate constants for depletion of triallylamine, obtained using the internal standard technique, are found to be independent of pressure and conversion, and fit the *Arrhenius* relationship

$$\log(k/s^{-1}) = 11.74 \pm 0.07 - (38.27 \pm 0.19)/\theta \quad \text{where } \theta = 2.303\,RT\ \text{kcal/mol}$$

The reaction appears to be homogeneous, as a 15-fold change in the surface-to-volume ratio of the vessel left the rate constants unchanged. The *Arrhenius* parameters are consistent with a molecular elimination reaction involving a six-center transition state, yielding propylene and N-allyl-prop-2-enaldimine. It is proposed that the latter product undergoes a 1,5-hydrogen transfer, followed by a ring closure reaction to yield dihydropicoline, which in turn reacts forming 3-picoline *via* a self-initiated decomposition reaction.

A. Introduction. – The thermal chemistry of organic nitrogen compounds has received only scant attention [1]. While the pyrolysis of alkylamines in general proceeds *via* radical chain mechanisms, recent investigations have shown that certain allylamines undergo interesting molecular elimination and rearrangement reactions. *Parry & Robinson* [2] demonstrated that the thermolysis of cyclopropylamine initially yields N-propylidene amine which is formed either by a concerted process or *via* a biradical intermediate. *Maccoll & Nagra* [3] and *Egger* [4] found that the thermal decomposition of N-*t*-butylacetamide and cyclohexylallylamine, respectively, undergo molecular rearrangement reactions *via* a six-center transition state, in analogous fashion to the reactions of oxygenated compounds such as allylethers, allylcarbinols and 'enoic' acids [5]. The thermal decomposition of allylamines also provides a simple, clean method of producing imines in the gas phase.

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