decolorized. The less soluble material, VIII, was isolated as white crystals, 1.5 g., m. p. 239–240°. The more soluble material was V. It was isolated as white crystals and recrystallized from butanol to give 6.6 g. (33%), m.p. 173–174°, carbonyl band at 5.92 μ.

Anal. Calcd. for $C_8H_5ClN_4O$: N, 26.87; Cl, 16.94. Found: N, 26.17; Cl, 16.6.

Type II.—Using a molar ratio of 1:1 of compounds I and VII with the conditions described earlier, the yield of V dropped to 5.0 g. (25%). No compound VIII was found.

B. Compound I as Solvent.—Into an erlenmeyer flask equipped with a magnetic stirrer and thermometer was placed 30.0 g. of I. The flask was warmed to 130°. Over a period of 45 min. 9.6 g. of VII was added. The yellow solution turned black and copious amounts of hydrogen chloride were evolved. The black melt was poured directly into a mortar, allowed to solidify, and ground to a fine powder. The powder (39.0 g.) was extracted for 4 hr. in a Soxhlet extractor. There remained after extraction 17.5 g. of the powder. This black powder was boiled in 500 ml. of Shellacol and filtered hot. The precipitate, 5.0 g., was a black solid, the bulk of which was not soluble in base, acid, nor the usual organic solvents. The hot Shellacol solution was treated with Norit and cooled. A black solid, 6.7 g., was separated. When recrystallized from butanol, using Norit as a decolorizing agent, there were produced white needles, 5.0 g. (25%), m.p. 173–174°.

C. Compound VII as Solvent.—In a three-necked flask equipped as described previously, was placed a finely ground mixture of 19.6 g. (0.2 mole) of VII and 14.9 g. (0.1 mole) of I. Once the internal temperature reached 118° the reaction became violent and exothermic. It was completed in 10 min. The black solid was removed from the flask, ground to a powder, and triturated consecutively with 3 *N* ammonium hydroxide, 300 ml. of Shellacol, and 300 ml. of ether. The black solid, 12.0 g., was extracted using a Soxhlet extractor for 48 hr. with dioxane. From the dioxane was isolated 1.3 g. of VI, m.p. 244–245°. None of compound V was isolated from the Shellacol fraction.

Acknowledgment.—The authors express their gratitude to Miss June Hyepock for preparation of several of the starting materials. The authors are indebted to the Analytical Staff of Riker Laboratories, Inc., Northridge, California, for providing analytical data.

The Pyrolysis of Pyrazineethanol and 2-Pyridineethanol

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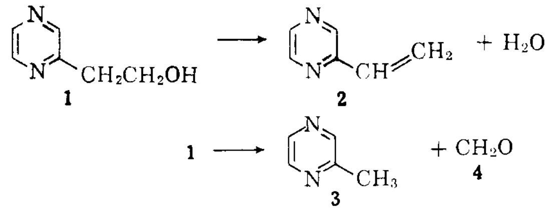
Gas chromatographic examination of a sample of pyrazineethanol (1) revealed the presence of small amounts of three lower boiling substances with retention-times corresponding to vinylpyrazine (2), methylpyrazine (3), and formaldehyde (4). On the assumption that these minor peaks did not represent impurities in 1 but were artefacts formed in the preheater ($T \sim 240°$) of the chromatography column according to equations 1 and 2, samples of 1 were chromatographed at progressively higher preheater temperatures giving correspondingly larger amounts of the more volatile substances. At a preheater temperature of 370° only about 20% of the injected sample emerged unchanged.

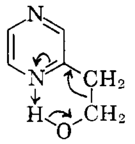


(1)

(2)

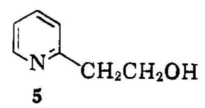
If the dehydration (equation 1) were the result of a base-catalyzed bimolecular elimination and the fragmentation (equation 2) that of a unimolecular reaction, a change in the preheater assembly should affect the ratios of the products formed. The glass wool in the preheater, serving as a site for bimolecular elimination, was removed leaving the preheater as a hot tube with greatly diminished surface area. Samples of 1 were then chromatographed giving only traces of decomposition at 225° and about 85% decomposition at 380°. From ratios of peak areas it was estimated that the decomposition proceeded almost exclusively (∼99%) *via* equation 2, whereas with a packed preheater about 10% of the decomposition proceeded *via* equation 1. That the decomposition products were in fact 2, 3, and 4 was established by comparison of derivatives, retention times, and physical measurements of collected samples.

Based on the foregoing observations the following mechanism involving a cyclic transition state was considered for the formation of 3 and 4 from 1.

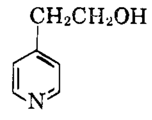


I

As a test of this hypothesis samples of 2-pyridineethanol (5) and 4-pyridineethanol (6) were chromatographed over a range of preheater temperatures. Compounds 1 and 5 are structurally analogous and should undergo an analogous pyrolytic breakdown, while 6, though electrically similar,[2] does not embody the structural features required for facile fragmentation.

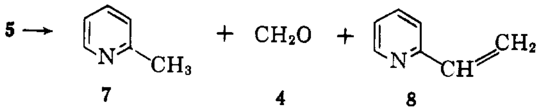


5



6

Samples of 5 were chromatographed at preheater temperatures of 195° to 390° giving the anticipated products (equation 3). As in the pyrolysis of 1, only traces of decomposition occurred at 195° with progressively more up to about 90% at 390°. In analogy to the pyrolysis of 1 about a per cent of 8 was formed. An additional small broad peak which emerged from the column prior to unchanged 5 was observed in the lower temperature runs and was shown to be 8, probably



(3)

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[1] (a) Research Associate, 1958–1960; (b) Medical Research Laboratories, Chas. Pfizer and Co. Inc., Groton, Conn.

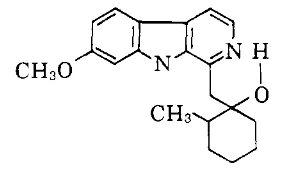
[2] For discussions of similarity between the pyridine 2- and 4-positions see (a) W. E. Doering and R. A. N. Weil, *J. Am. Chem. Soc.*, **69**, 2461 (1947) and (b) H. S. Mosher, "The Chemistry of the Pyridines" in Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 397.

formed by dehydration of **5** during passage through the column.

The decomposition pattern seen in the chromatograms of **1** and **5** was not shown by 4-pyridineethanol (**6**). Samples of **6** were chromatographed at temperatures of 190° to 355° giving over the entire range about 5% decomposition to 4-vinylpyridine, as seen in the appearance of a broad peak emerging prior to unchanged **6**. The increased amount of column dehydration of **6** over **5** is consistent with the possibility that the amines themselves catalyzed the dehydrations. At 355° there was only a suggestion of decomposition of **6** in the preheater. The pattern of small peaks indicated that the fragmentations at this temperature might be going *via* a different mechanism.[3]

Although these experimental findings do not rigorously establish the mechanism or pyrolytic breakdown of **1** and **5**, they are consistent with the postulated cyclic transition state. The assumption of a unimolecular mechanism is supported by (1) the observation that higher preheater temperatures (which would lead to increased vaporization of the injected samples) led to increased decomposition of **1** and **5** without affecting **6**, (2) the fact that both **5** and **6** are easily dehydrated when heated in the liquid state,[4] and (3) reports that **1**, **5**, and **6** are smoothly converted to the corresponding olefins when heated in the presence of potassium hydroxide.[5,6]

The enamines of **3** and **7** which would be formed directly in the pyrolyses of **1** and **5** are thought to tautomerize rapidly upon contact with the column packing. The proposed cyclic transition state is directly analogous to many of those from the ever-increasing catalog of reactions which are postulated to occur *via* 6-ring transition states. In another closely analogous reaction it has been shown that the carbinol **9** is converted to harmine and 2-methylcyclohexanone upon being heated in a test tube at 240°.[7] This interesting degradation was explained in terms of the same 6-ring transition state as was postulated before, although the possibility of a bimolecular reaction in the melt is not excluded.



9

Experimental[8]

Gas Chromatography. Pyrolysis.—The pyrolyses were carried out in the preheater section of a conventional gas chromatography apparatus. The short (12 × 90 mm.) glass preheater was heated by an external spiral of resistance wire. Preheater (pyrolysis) temperatures are probably correct to about ±10° (external thermocouple). Helium was used at a flow rate of about 60 cc./min. A U-shaped Pyrex column (8 mm. o.d. × 7 ft.) was packed to a point 5 cm. from the preheater section. The column packing consisted of 30% of Dow-Corning "550" silicone fluid on Johns-Manville 60/80-mesh Chromosorb which had been pretreated with 3% methanolic potassium hydroxide. The exit to the detector block was constructed so as to facilitate sample collection in Dry Ice-cooled capillaries.

Materials.—Methylpyrazine (Wyandotte), and 2- and 4-methylpyridine (Eastman) were used without further purification. 2-Pyridineethanol (Aldrich) was purified by distillation, $n^{25}\text{D}$ 1.5359 (lit.[5a] $n^{20}\text{D}$ 1.5374). The picrates of these substances were prepared in the usual way. Methylpyrazine picrate (ethyl acetate) had m.p. (capillary) 129–131° (lit.[9] m.p. 133°). 2-Mehtylpyridine picrate (methanol) had m.p. (capillary) 166–167.5° (lit.[10] m.p. 165°). 2-Pyridineethanol picrate (ethyl acetate) had m.p. (hot stage) 120.5–121° (lit.[11] m.p. 120–121°).

Pyrazineethanol was prepared according to Kitchen and Hanson.[5a] The pure material (b.p. 84° at 0.5 mm.) had $n^{25}\text{D}$ 1.5362 lit.[5a] n^{25})D 1.5378); picrate (ethyl acetate), m.p. (hot stage) 73–74°.

Anal.[12] Calcd. for $C_{12}H_{11}O_8N_5$: C, 40.80; H, 3.14; N, 19.83. Found: C, 40.84; H, 3.18; N, 20.13.

Vinylpyrazine was available in 80% yield from pyrazineethanol.[5a] The pure olefin had $n^{25}\text{D}$ 1.5542 (lit.[5a] $n^{20}\text{D}$ 1.5565); picrate (ethanol), m.p. (capillary) 100–101.5° dec. (lit.[5a] m.p. 101°). Ultraviolet spectrum (ethanol): 229.5 mμ, ϵ 12,900; 286.5 mμ, ϵ 6900. The olefin instantly decolorized 2% permanganate whereas pyrazineethanol did not.

4-Pyridineethanol was prepared from 4-methylpyridine and formalin,[13] $n^{24}\text{D}$ 1.5410 (lit.[14] $n^{25}\text{D}$ 1.5388), m.p. 8–9.5° (lit.[14] m.p. 13.1–13.3°); mol. wt., 123 (mass spectrum)[15]; m.p. (hot stage) 133–134.5° (lit.[5b] m.p. 134–135°).

4-Vinylpyridine[14] was synthesized from 4-pyridineethanol by distillation from potassium hydroxide at 130°. The pure olefin had $\lambda_{\max}^{\mathrm{EtOH}}$ 243 mμ; picrate (benzene), m.p. (capillary) (135–160° changed form) 200–204° dec. (lit.[5b] m.p. 198–199° dec., sintering at 158–165°).

Pyrolysis of Pyrazineethanol (Preliminary Runs).—Preheater (pyrolysis section) was packed with glass wool; column *T*, 205°; sample size, 2 μl. Pyrazineethanol was chromatographed at preheater temperatures of 245, 285, 315, 350, and 370° giving trace, trace, 10, 50, and 80% decomposition, respectively.[16] New peaks appeared at retention times corresponding to those of air (a triplet with one major peak), methylpyrazine, and vinylpyrazine. Ratios of peak areas of vinylpyrazine to methylpyrazine were 3, 1, and $^1/_9$ at pyrolysis temperatures of 245, 285, and 370°, respectively.

Pyrolysis of Pyrazineethanol (Final Runs).—Preheater was empty; column *T*, 190°; sample size 6 μl. Pyrazineethanol was chromatographed unchanged at preheater *T*, 190° (infrared spectrum of eluate, retention time 13.6 min.). Pyrazineethanol was then chromatographed at preheater temperatures of 225, 265, 305, 340, 360, and 380° giving <1, <1, 10, 30, 60, and 85% decomposition, respectively, to increasing amounts of two substances with retention times of 0.8 and 2.7 min. The first peak (0.8 min.) was identified as formaldehyde by passage of the effluent helium through 3 ml. of an aqueous dimedon solution and

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[3] Phenethyl alcohol exhibited a similar decomposition pattern at preheater temperatures of 345–390°. For pyrolysis of phenethyl alcohol, see L. R. Herndon and E. E. Reid, *J. Am. Chem. Soc.*, **50**, 3066 (1928).

[4] E. Profft, *Chem. Tech.* (Berlin), **8**, 378 (1956).

[5] (a) L. J. Kitchen and E. S. Hanson, *J. Am. Chem. Soc.*, **73**, 1838 (1951); (b) J. Meisenheimer, J. Neresheimer, and W. Schneider, *Ann.*, **420**, 190 (1920).

[6] *Cf.* J. D. Behun and R. Levine, *J. Am. Chem. Soc.*, **81**, 5666 (1959), who have demonstrated a base-catalyzed reversal in the substituted pyrazineethanol series (1,1-diphenylpyrazineethanol) where the steric requirements favored the reversal (to methylpyrazine and benzophenone) rather than dehydration.

[7] C. F. Huebner, H. B. MacPhillamy, A. F. St. André, and E. Schlittler, *J. Am. Chem. Soc.*, **77**, 472 (1955).

[8] Melting points were taken on a Kofler hot-stage microscope or in open capillaries (as noted) and are not corrected.

[9] C. Stoehr, *J. prakt. Chem.*, **51**, 464 (1895).

[10] A. Ladenburg, *Ann.*, **247**, 7 (1888).

[11] W. Koenigs and G. Happe, *Ber.*, **35**, 1343 (1902).

[12] Microanalysis by S. M. Nagy, Massachusetts Institute of Technology.

[13] E. E. Mikhlina and M. V. Rubtsov, *Zh. Obshch. Khim.*, **28**, 103 (1958); *Chem. Abstr.*, **52**, 12864 (1958).

[14] H. C. Brown and N. R. Eldred, *J. Am. Chem. Soc.*, **71**, 445 (1949).

[15] The author is grateful to Prof. Biemann for this spectrum and interpretation.

[16] As approximated by decrease in area of the peak corresponding to pyrazineethanol, 2- or 4-pyridineethanol.

isolation (after 16 hr.) of formaldimedon (ethanol–water), m.p. 192–192.5°, pure or mixed with an authentic sample. The second peak (2.7 min.) was condensed in a small capillary and identified as methylpyrazine; infrared spectrum (carbon tetrachloride) identical with that of authentic material; picrate (ethyl acetate), m.p. 127°, softening at 128.5–130.5°, pure or mixed with an authentic sample of methylpyrazine picrate (m.p. 129–131°).

A third peak corresponding in retention time (4.1 min.) to vinylpyrazine built up gradually to about 1% yield at 380°. Collection of this substance did not afford enough material for derivative formation, but instantaneous decoloration of permanganate provided additional support for the assignment of vinylpyrazine to this peak.

Pyrolysis of 2-Pyridineethanol.[17]—Preheater was empty; column T, 190°; sample size, 6 μl. 2-Pyridineethanol was chromatographed essentially unchanged[18] at preheater T, 190° (infrared spectrum of eluate, retention time 11.2 min.). 2-Pyridineethanol was then chromatographed at preheater temperatures of 195, 230, 265, 285, 310, 340, 370, and 390° giving <1, ~ 1, 5, 10, 35, 55, 70, and 90% decomposition, respectively, to increasing amounts of two substances with retention times of 0.8 and 2.6 min. The first peak (0.8 min.) was identified as formaldehyde by conversion to formaldimedon (see preceding). Second peak (2.6 min.) was identified as 2-methylpyridine; infrared spectrum (chloroform); picrate (methanol), m.p. 165°, softening at 166–167°, pure or mixed with an authentics ample of 2-methylpyridine picrate. A third peak of retention time 4.0 min. built up gradually to about 1% yield at 370–390°. Two collections of this substance did not afford material for derivative formation. This material decolorized permanganate instantly and showed $\lambda_{\max}^{\mathrm{EtOH}}$ 235 mμ,[19] thereby supporting the assignment of 2-vinylpyridine to this peak. A fourth broad peak, retention time 5.4–8.4 min., was present in the low-temperature runs but diminished in intensity at higher temperatures. Small samples were collected from 215° runs. This material decolorized permanganate instantly and showed $\lambda\lambda_{\max}^{\mathrm{EtOH}}$ 235 and 277.5 mμ.[19] An infrared spectrum (very weak, cavity cell, chloroform) showed all of the major bands for 2-vinylpyridine.[20]

Pyrolysis of 4-Pyridineethanol.—Preheater was empty; column T, 190°; sample size, 6 μl. 4-Pyridineethanol was chromatographed at temperatures of 190, 240, 280, 320, and 355° giving over the entire range about 5% decomposition to a low, broad peak of retention time 6.8–13.6 min. At 355° there was only a small amount (~ 1%) of decomposition in the preheater to form peaks with retention times of 0.8, 1.0, 2.8, 3.2, 3.7, and 5.1 min.—a pattern which was qualitatively similar to that from a sample of phenethyl alcohol.[4] The main peak, retention time 18.4 min., was collected and identified as unchanged 4-pyridineethanol (infrared spectrum, chloroform). Material collected from the broad peak decolorized permanganate instantly and showed $\lambda_{\max}^{\mathrm{EtOH}}$ 243 mμ. An infrared spectrum (weak, cavity cell, chloroform) showed all of the major bands for 4-vinylpyridine.

Pyrazineethanol and 2-pyridineethanol[21] can form strong intramolecular H-bonds. It is interesting to compare the retention times of pyrazineethanol (13.6 min.) and 2-pyridineethanol (11.2 min.) with that of 4-pyridineethanol (18.4 min.) which cannot form an intramolecular H-bond.[22]

Acknowledgment.—The author is indebted to Dr. Max Stoll of Firmenich et Cie., Geneva, for generous financial support, to Dr. F. D. Greene for helpful discussions, and to Professor G. Büchi for many useful suggestions and continuing encouragement.

[17] In a preliminary run with a preheater packed with glass wool 2-pyridineethanol was chromatographed over a range of preheater temperatures. The decomposition was analogous to that from the corresponding series with pyrazineethanol: new peaks emerged at retention times corresponding to air, methylpyridine, and 2-vinylpyridine (estimated; no comparison with authentic material).

[18] Small peaks (~ 1%) at 4.0 and 5.8–8.4 min.

[19] Sample rinsed from collection capillary directly into cuvette. R. P. Mariella, L. F. A. Peterson, and R. C. Ferris, *J. Am. Chem. Soc.*, **70**, 1494 (1948), report for 2-vinylpyridine $\lambda_{\max}$ 235 mμ, log ϵ 4.1, and $\lambda_{\max}$ 278, mμ, log ϵ 3.7.

[20] Satdler curve #6654.

[21] P. R. Schleyer, C. Wintner, D. S. Trifan, and R. Bacskai, *Tetrahedron Letters*, **14**, 1 (1959), report for 2-pyridineethanol $\Delta\nu = 205$.

[22] C. H. DePuy and P. R. Story, *Tetrahedron Letters*, **6**, 20 (1959), report that internal H-bonding decreases retention time.

A Convenient Separation of *cis*- and *trans*-Methoxycyclohexanols

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Received March 12, 1963

A recent communication[2] regarding the separation of *cis*- and *trans*-cycloalkanediols by means of *n*-butylboronic acid prompts us to report some observations made about two years ago regarding the separation of the corresponding monoalkyl ethers by means of a lithium aluminum hydride–aluminum chloride reagent.[3] In attempts to equilibrate the epimeric 4-methoxycyclohexanols by this reagent (presumably[4,5] $AlHCl_2$) as previously described for the corresponding 4-methylcyclohexanols[6] we observed the immediate formation of a granular precipitate when ethereal solutions of the two alcohols were mixed with similar solutions of the hydride reagent. When the precipitate was collected, washed with ether, and then slurried with fresh ether and treated with 10% aqueous sulfuric acid, the 4-methoxycyclohexanol recovered from the ether layer was almost exclusively (>95%) the *cis* isomer as indicated by gas chromatographic analysis and preparation of the known[7] crystalline *p*-toluenesulfonate. In contrast, decomposition of the ethereal filtrate with 10% sulfuric acid led to *trans*-4-methoxycyclohexanol, identified by its crystalline hydrogen phthalate,[7] and shown, gas chromatographically, to be 87% isomerically pure.

Similar results were obtained with the 3-methoxycyclohexanols. Here, again, the precipitated material returned mainly *cis*-3-methoxycyclohexanol (90% pure by gas chromatography), identified by its hydrogen phthalate,[8] whereas the filtrate yielded the hitherto unknown *trans*-3-methoxycyclohexanol, characterized as its 3,5-dinitrobenzoate, in over 99% purity.

It was further observed that: (a) no separation occurred with the 2-methoxycyclohexanols (a precipitate formed but, upon decomposition, it yielded a mixture of isomers identical with the starting mixture); (b) the 4-methoxycyclohexanols yielded no precipitate with aluminum chloride alone and with lithium aluminum hydride alone they gave rise to a different precipitate which lead to little separation of isomers; (c) for obvious reasons, no precipitate formed from very *trans*-rich mixtures of 4-methoxycyclohexanol.

The previous observations may be explained readily if it is granted that the granular precipitates are intramolecular chelates as depicted in Fig. 1. Clearly such chelates can form only from the *cis*-4 and *cis*-3 isomers (not the corresponding *trans* forms), but presumably

[1] The Radiation Laboratory is operated under contract with the U. S. Atomic Energy Commission. This note is taken in part from the Ph.D. dissertation of T. J. B.

[2] H. C. Brown and G. Zweifel, *J. Org. Chem.*, **27**, 4708 (1962).

[3] *Cf.* E. L. Eliel, *Rec. Chem. Progr.*, **22**, 129 (1961).

[4] E. Wiberg and M. Schmidt, *Z. Naturforsch.*, **6b**, 460 (1951).

[5] G. G. Evans, J. K. Kennedy, and F. P. Del Greco, *J. Inorg. Nucl. Chem.*, **4**, 40 (1957).

[6] E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960).

[7] D. S. Noyce, G. L. Woo, and B. R. Thomas, *J. Org. Chem.*, **25**, 260 (1960).

[8] D. S. Noyce, B. R. Thomas, and B. N. Bastian, *J. Am. Chem. Soc.*, **82**, 885 (1960).