illustrated elsewhere[31] reveal a nonlinear relationship between Z value and salt concentration, especially in nonpolar solvents. Electrochemical studies were carried out with a Heath polarographic apparatus (Heath Co., Benton Harbor, Mich.). Fast scans were performed with a Hewlett-Packard function generator 3300A and Tektronix oscilloscopes (532 or 564). The polarographic cells used were like those described by Schwarz[29] or a simpler H type. The counterelectrode was platinum wire (22 gauge) sealed into soda glass. The working electrode was either a dropping mercury type (Sargent and Co., "2–5 sec" capillary) or a hanging mercury drop. All polarographic measurements were made with the same capillary and at the same head of mercury. Potentials are referred to (silver wire) $Ag/AgClO_4$ (0.01 *M*) in CH_3CN (0.1 *M* tetra-*n*-butylammonium perchlorate). (This reference system is easier to use than the saturated calomel electrode (sce).) Solutions were deoxygenated with nitrogen passed over BTS catalyst (Badische Anilin und Sodafabrik, Ludwigshafen-am-Rheim, Germany) at 120°, through a deep blue solution of methylviologen cation radical[32] in CH_3CN, and through CH_3CN over molecular sieve 4A and Drierite. The system was calibrated against a mercury cell (1.35 V) before and after each experiment. The scan rate was checked against a previously recorded 100-mV change.

Acknowledgments. We are grateful for valuable discussions with Professor Harold L. Friedman of our department and with Professor Joshua Jortner, Department of Chemistry, Tel-Aviv University. The kindness of Dr. C. Beguin and Professor J. J. Delpuech (Institut de Chimie, Universite, Nancy, France) in supplying 4-nitrobenzyl fluoride is appreciated. Grateful acknowledgment for support is made to the National Institutes of Health, the Army Research Office (Durham), the Petroleum Research Fund (PRF-3695AI), Edgewood Arsenal, and the National Science Foundation.

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N-Alkoxypyridinium Salts from Amine Oxides and Epoxides. Preparation, Reactions, and Mechanism of Base-Induced Decomposition[1,2]

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Abstract: Aromatic amine oxides react readily with epoxides in nitromethane in the presence of strong, nonnucleophilic acids to yield *N*-alkoxypyridinium salts. Several adducts of 2,6-lutidine *N*-oxide with styrene oxide and 1,2-epoxycyclohexane have been obtained as analytically pure solids as the perchlorate (**3a**, **5a**, **5c**) and the fluoroborate salts (**3b**, **5b**). The perchlorate salt of 2,6-lutidine *N*-oxide with 1,2-epoxybutane has also been prepared. An adduct of 2,4-lutidine *N*-oxide, 1,2-epoxycyclohexane, and perchloric acid has been isolated as its acetylated derivative (**6**). These salts undergo base-induced decomposition to the amine and carbonyl compounds; in addition, the styrene oxide adducts are susceptible to nucleophilic substitution with displacement of the amine oxide moiety. Deuterium-labeling experiments indicate that base-induced decomposition of *N*-(2-acetoxycyclohexyloxy)-2,6-lutidinium perchlorate (**5c**) and of *N*-methoxy-2,6-lutidinium iodide (**9**) to 2,6-lutidine and the respective carbonyl compounds does not occur by direct abstraction of the α proton, to any detectable extent. Instead, the α proton is transferred to a ring methyl group by an intramolecular process involving N–O bond cleavage. Since it also is demonstrated that a ring methyl group proton is removed reversibly to give an ylide, it is likely that the α proton is transferred to the carbanionic center of that ylide.

Virtually no literature exists on the reactions of amine oxides with epoxides, though there is a plethora of reactions of epoxides with other nucleophiles.[5] The one reported study[6] demonstrated only that some oxygen transfer occurs and, under the vigorous reaction conditions used, mixtures of products were obtained in low yield with no isolation of intermediates. The present research was initiated (a) to determine the scope of the reaction of aromatic amine oxides with epoxides in the presence of strong, nonnucleophilic acids; (b) to elucidate pathways of decomposition of the intermediate *N*-alkoxypyridinium salts, with particular attention to the mechanism of base-induced decomposition, using deuterium labeling; and (c) to ascertain the products of thermal and base-induced decomposition of the intermediate alkoxypyridinium salts.

Aromatic amine oxides are highly dipolar species. The dipole moment of pyridine *N*-oxide (in benzene, 25°) is 4.24 D,[7] a value close to those of dimethyl sulfoxide (4.3),[8] nitromethane (3.99),[8] and dimethylformamide (3.82).[9] Because of the tight negative

(1) Chemistry of Epoxides. XXVII. XXVI: *J. Amer. Oil Chem. Soc.*, **47**, 424 (1970).

(2) Presented in part at the Fourth Middle Atlantic Regional Meeting, Washington, D. C., Feb 1969, and at the 159th Meeting of the American Chemical Society, Houston, Texas, Feb 1970.

(3) Work done in partial fulfillment of the Ph.D. degree, Temple University, 1970.

(4) To whom all correspondence should be addressed.

(5) André Rosowsky in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part One, Arnold Weissberger, Ed., Interscience, New York, N. Y., 1964, p 230 ff.

(6) R. Oda, Y. Hayashi, and T. Yoshida, *Nippon Kagaku Zasshi*, 87, 975, 978 (1966); *Chem. Abstr.*, **65**, 16923*b*, 19960*e* (1966).

(7) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., Amsterdam, 1967, p 78.

(8) A. J. Parker, *Quart. Rev., Chem. Soc.*, 163 (1962).

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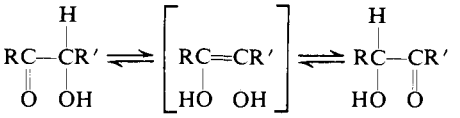
charge cloud on oxygen, amide oxides behave as hard bases; they are easily protonated and prefer organic substrates with highly electrophilic, partially positively charged centers (hard acids).[10,11] They may also be readily alkylated, as we shall demonstrate in this paper, by protonated epoxides.

In 1913, it was observed that trimethylamine *N*-oxide reacts with methyl iodide to generate an alkoxyammonium salt, which can subsequently be decomposed by base to give formaldehyde and trimethylamine (eq 1).[12] Quinoline *N*-oxide was later shown to behave in

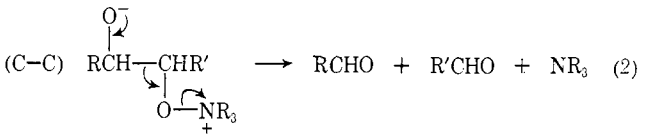
$$Me_3\overset{+}{N}-O + MeI \longrightarrow [Me_3\overset{+}{N}-O-Me]I^- \xrightarrow{OH^-} Me_3N + HCHO \quad (1)$$

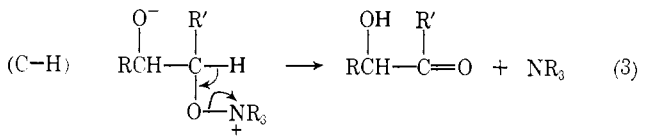
the same way.[13] Amine oxides were found capable of being alkylated by alkyl tosylates[14] and by methyl sulfate.[15]

In the one investigation of the reaction of amine oxides with epoxides,[6] reaction processes may be inferred from isolated derivatives of reaction products. Reactions were carried out at elevated temperatures and proceeded equally well with or without catalytic amounts of acid (BF_3). The same α-ketols resulted with or without acid catalysis, it was suggested, because of the interconversion



The reaction products isolated[6] show the influence of the OH functionality in directing carbon–carbon (C–C) as well as carbon–hydrogen (C–H) bond cleavage in epoxide adducts (proposed intermediates are shown in eq 2 and 3). No attempt was made, however, to isolate intermediates or to examine them spectrally.

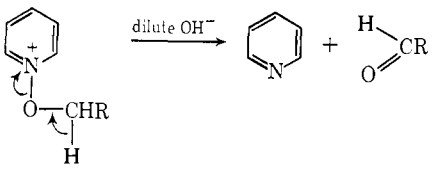




In a recent report, the reactions of *N*-alkoxypyridinium salts with various nucleophiles are summarized.[16] Reactions are divided into four categories, one of which is particularly relevant to this work (Scheme I). The present study will demonstrate that such decomposition need not occur *via* direct α-proton abstraction when other pathways exist.

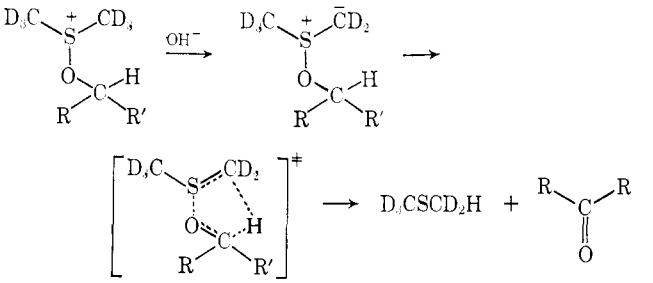
Precedents exist for the suggestion that direct proton abstraction need not occur, as shown in studies with analogous *S*-alkoxydimethylsulfonium salts,[17] which

Scheme I



decompose thermally or in base to an alkyl sulfide and a carbonyl compound. In these cases, α-proton abstraction may be preceded by ylide formation. Subsequently, intramolecular hydrogen transfer occurs during the rearrangement to a carbonyl compound and an alkyl sulfide *via* a suggested five-membered cyclic transition state (Scheme II).

Scheme II



Experimental Section

Infrared spectra were determined using a Perkin-Elmer Infracord spectrophotometer. Ultraviolet spectra were recorded on a Perkin-Elmer 202 ultraviolet-visible spectrophotometer. Nuclear magnetic resonance spectra were determined using a Varian A-60A instrument; tetramethylsilane (tms) was used as an internal standard, except in aqueous solutions, wherein sodium 2,2-dimethyl-2-silapentane-5-sulfonate (dss) was used instead. Gas–liquid phase chromatography (glpc) was performed on an F & M Model 500 programmed temperature gas chromatograph.

Aquametry was carried out using a Labindustries aquametry apparatus and Harleco Karl Fischer Reagent freshly standardized with known amounts of water. Potentiometric titrations were done with a Leeds and Northrup Model 7401 stabilized pH indicator equipped with a Thomas Model 4858-L15 combination electrode.

Thin-layer chromatograms were done on Eastman silica gel chromatograms with fluorescent indicator. Spots were visualized under ultraviolet light and by developing with iodine vapor. Column chromatographs utilized Baker Analyzed Reagent grade silica gel or Mallinckrodt Analyzed Reagent grade 100 mesh silicic acid.

For drying, Fisher Certified Reagent grade anhydrous magnesium sulfate, sodium sulfate, or Linde Molecular Sieves Type 4A (activated at 450°) was used.

2,6-Lutidine, 2,4-lutidine, and all amine oxides except 2,4-lutidine *N*-oxide were samples from the Reilly Tar and Chemical Corp. and were purified by spinning-band column distillation. Styrene oxide (**2**) (Aldrich), 1,2-epoxycyclohexane (**4**) (Columbian Carbon Co.), and nitromethane (Eastman) were each distilled on a spinning band column at a reflux ratio 20:1. 1,2-Epoxybutane (Aldrich), fluoroboric acid (48–50%) (Baker), perchloric acid (70%) (Mallinckrodt), trifluoroacetic acid (Eastman), *p*-toluenesulfonic acid (Eastman), isopropenyl acetate (Aldrich), styrene glycol (Baker), *cis*- and *trans*-1,2-cyclohexanediol (Pfaltz and Bauer), and 2-hydroxyacetophenone (Eastman) were used without additional purification. Pyridine (Mallinckrodt) was distilled from calcium oxide and stored over potassium hydroxide pellets. Adipoin (2-hydroxycyclohexanone) (**7a**) was generated by destructive distillation of adipoin dimer (Pfaltz and Bauer).[18] Harleco stan-

(10) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962).
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(17) (a) A. H. Fenselau and J. G. Moffatt, *J. Amer. Chem. Soc.*, 88, 1762 (1966); (b) K. Torsell, *Tetrahedron Lett.*, 4445 (1966); (c) F. W. Sweat and W. W. Epstein, *J. Org. Chem.*, **32**, 835 (1967); (d) C. R. Johnson and W. G. Phillips, *ibid.*, **32**, 1926 (1967).
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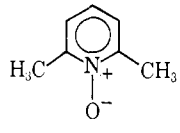
dardized 0.100 *N* sodium hydroxide solution was used for titrations.

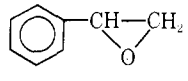
The following deuterated materials were used without further purification, unless so indicated; isotopic purities are given in parentheses: D_2O (99.8%) (Diaprep) (>99% by nmr analysis, using pyridine as an internal standard), pyridine-d_5 (99%) (Aldrich) (stored over Molecular Sieves Type 4A), nitromethane-d_3 (>99%) (Diaprep) (stored over Molecular Sieves Type 4A), chloroform-*d* (>99.8%) (Diaprep), and 40% NaOD in D_2O (Merck, Sharp and Dohme).

2,6-Dimethyl-d_6-pyridine *N*-Oxide (1-d_6). 2,6-Lutidine *N*-oxide (**1**) (5.00 ml) was placed in a Mini-lab round-bottom flask equipped with a condenser and a bubbler with Nujol to isolate the system from atmospheric moisture. NaOH (two pellets) and D_2O (4.74 ml) (2 equiv of deuterium per equivalent of exchangeable protium) were added, and the contents heated for 2 hr at 130°. A side condenser was attached and most of the water distilled off; the residue in the flask consisted of **1** and wet NaOD. A fresh charge of D_2O was added and the procedure repeated. After four charges of D_2O, >98% of the protium on the methyl groups had been replaced with deuterium, as determined by nmr analysis. The remaining water was removed under vacuum at 30° (12 Torr). The temperature was then raised until the product distilled, 120–122° (9.5 Torr).

This procedure is adapted from the literature.[19] Aromatic protons do not exchange as shown by the nmr spectra of epoxide adducts in which the ratio of the para to the meta signal is the expected 1:2 ratio.



1



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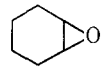

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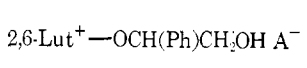
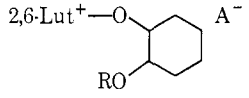
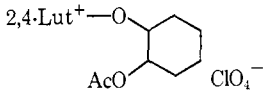


3a, $A^- = ClO_4^-$
b, $A^- = BF_4^-$ [Lut = *N*-lutidyl]
c, $A^- = CF_3CO_2^-$



5a, $A^- = ClO_4^-$; R = H
b, $A^- = BF_4^-$; R = H
c, $A^- = ClO_4^-$; R = Ac



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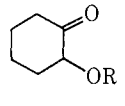


7a, R = H
b, R = Ac

Amine Oxide–Acid Salts. Table I gives pertinent data on amine oxide–acid salts prepared in this work. All filtrations described in this paper were carried out on sintered glass filters. Equivalent weights were determined by titration in aqueous solution with 0.100 *N* sodium hydroxide to a phenolphthalein end point. Salts were prepared by adding the proper molar ratio of amine oxide and acid to ethanol, precipitating the crude product by addition of ether, and recrystallizing the crude precipitate from ethanol. Attempted recrystallization of the 1:1 **1**·$HClO_4$ salt gave only the 2:1 salt. Attempts to isolate salts of **1** with trifluoroacetic acid and with trichloroacetic acid failed.

2,6-Lutidine *N*-Oxide–Styrene Oxide Adducts (3). In a representative run, (**1**)$_2$·$HClO_4$ (2.00 g, 5.76 mmol) was dissolved in nitromethane (4.36 ml, 80.7 mmol). The resulting solution was warmed to 37° and treated with styrene oxide (**2**) (1.32 ml, 11.5 mmol) added dropwise with stirring. After 1 hr, the solution was cooled and the adduct precipitated by the addition of ether. Trituration with ether changed the consistency of the precipitate from a paste to a powder; the crude adduct was then purified by crystallization from acetone–ether: yield of the perchlorate adduct (**3a**), 1.23 g (62%), mp 104–105°.

Anal. Calcd for $C_{15}H_{18}NO_6Cl$: C, 52.41; H, 5.28; N, 4.07; Cl, 10.31. Found: C, 52.68; H, 5.32; N, 4.33; Cl, 10.49.

(19) C. W. Muth, R. S. Darlak, M. L. DeMatte, and G. F. Chovanec, *J. Org. Chem.*, **33**, 2762 (1968).

Table I. Amine Oxide–Acid Salts

Formula[e]	Mp, °C	Equiv wt Found	Equiv wt Calcd
(2,6-Lut-O)$_2$·$HClO_4$	187.5–188[a,b]		
2,6-Lut-O·$HClO_4$	144–145	226[c]	224
(4-Pic-O)$_2$·$HClO_4$	80.5–83[d]		
(2-Pic-O)$_2$·$HClO_4$	133–134[e]		
(Py-O)$_2$·HBF_4	73.5–74.5	269	278
(Py-O)$_2$·$HClO_4$	77.5–78.5	296[c]	291
(2,6-Lut-O)$_2$·HBF_4	179–180	335	334
2,6-Lut-O·*d*-camphorsulfonic acid	138.5–140.4	367	355
(2,6-Lut-O-)$_2$·picric acid	96.2–97.3	457	475
2,6-Lut-O·*p*-toluenesulfonic acid	145–146	297	295
2,6-Lut-O·0.5H_2SO_4	139–140	170	172
(2,4-Lut-O)$_2$·$HClO_4$	112–113.5	350	348

[a] Lit. mp 185.5–187°: C. W. Muth and R. S. Darlak, *J. Org. Chem.*, **30**, 1909 (1965). [b] Lit. mp 185.5–186°: M. Szafran, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **11**, 111 (1963). [c] Determined potentiometrically. [d] Lit. mp 76–77° (footnote *b*). [e] Abbreviations: Lut-O = lutidine *N*-oxide; Pic-O = picoline *N*-oxide; Py-O = pyridine *N*-oxide.

The fluoroborate adduct was prepared by the same procedure, using (**1**)$_2$·HBF_4: yield of the fluoroborate adduct (**3b**), 37%, mp 100.7–101.2°.

Anal. Calcd for $C_{15}H_{18}NO_2BF_4$: C, 54.41; H, 5.48; N, 4.23. Found: C, 54.66; H, 5.32; N, 4.15.

Adducts (5) from 2,6-Lutidine *N*-Oxide and 1,2-Epoxycyclohexane. In a representative run, (**1**)$_2$·$HClO_4$ (27.5 g, 79.3 mmol) was dissolved in nitromethane (64.3 ml, 1.19 mol). The resulting solution was stirred at 37° while 1,2-epoxycyclohexane (**4**) (15.6 g, 159 mmol) was added dropwise. After 1 hr, the reaction mixture was chilled and the adduct was precipitated by addition of ether. Recrystallization of the precipitate from absolute ethanol gave the pure product: yield of the perchlorate adduct (**5a**), 22.4 g (88%), mp 124–125°; recrystallized for analysis, mp 125–126°.

Anal. Calcd for $C_{13}H_{20}NO_6Cl$: C, 48.53; H, 6.26; N, 4.35; Cl, 11.02. Found: C, 48.75; H, 6.08; N, 4.41; Cl, 11.07.

The fluoroborate adduct was prepared by the same procedure, using (**1**)$_2$·HBF_4: yield of the fluoroborate adduct (**5b**), 59%, mp 124–125°; recrystallized for analysis, mp 125–126°.

Anal. Calcd for $C_{13}H_{20}NO_2BF_4$: C, 50.51; H, 6.52; N, 4.53. Found: C, 50.61; H, 6.30; N, 4.61.

2,6-Lutidine *N*-Oxide–1,2-Epoxybutane Adduct (8). 1,2-Epoxybutane (0.843 g, 11.7 mmol) was used without purification. It was added dropwise to a solution of (**1**)$_2$·$HClO_4$ (2.03 g, 5.84 mmol) in nitromethane (4.74 ml, 87.7 mmol) at 41° and the reaction then allowed to proceed for 1 hr at that temperature. Ether trituration and vacuum desiccation left a somewhat sticky solid which was seen by ir analysis to contain a large amount of unreacted (**1**)$_2$·$HClO_4$. By recrystallization from absolute ethanol, 25% of this amine oxide–acid salt was recovered (mp 180–183° *vs.* 187–188° for authentic material; infrared spectrum identical with that of authentic material).

The residue from the mother liquor once again was crystallized from ethanol to give the adduct (0.395 g, 23% yield), mp 77.5–79.5°. Nmr analysis showed this to be contaminated with 3% (molar) of amine oxide.

One more recrystallization from ethanol gave 0.295 g (18% yield) of the pure product, mp 81.5–82.5°, free from amine oxide by nmr.

Anal. Calcd for $C_{11}H_{18}NO_6Cl$: C, 44.68; H, 6.14; N, 4.74; Cl, 11.99. Found: C, 44.95; H, 6.08; N, 4.75; Cl, 11.89.

Adduct Acetylation. **5a** (6.0 g, 18.6 mmol) was suspended in isopropenyl acetate (20 ml, 186 mmol). A trace of *p*-toluenesulfonic acid monohydrate was added and the mixture stirred at 70° for 0.5 hr. The original suspension quickly became a monophase. Volatiles then were removed under water aspirator vacuum; the brown residue was decolorized in chloroform with Norit A. Recrystallization of the product from absolute ethanol gave 6.3 g (93% yield) of the acetylated adduct, **5c**, mp 144.5–146°.

Anal. Calcd for $C_{11}H_{22}NO_7Cl$: C, 49.52; H, 6.10; N, 3.85; Cl, 9.75. Found: C, 49.69; H, 5.86; N, 4.04; Cl, 9.75.

2,4-Lutidine *N*-Oxide–1,2-Epoxycyclohexane Adduct. Acetylated Derivative (6). (2,4-Lutidine *N*-oxide)$_2$·$HClO_4$ (8.1 g, 23

mmol),[20] **4** (4.8 ml, 46 mmol), and nitromethane (19 ml, 355 mmol) were stirred for 1 hr at 44°. Ether extraction removed the nitromethane, excess epoxide, some excess amine oxide, and only a small amount of adduct (nmr analysis). However, the remaining material, an oil, could not be crystallized from ethanol or nitromethane, nor by trituration with ethyl acetate. Nmr analysis showed the mixture to be 72% adduct and 28% amine oxide (mole per cent).

The crude product was passed through a 1 ft long, 1 in. diameter column of silicic acid by adding a nitromethane solution to the column wet with nitromethane, and then eluting with ethyl acetate. The amine oxide was retained on the column, but the eluted material, apparently pure adduct by nmr analysis, still did not crystallize.

The viscous adduct was heated with a large excess of isopropenyl acetate and a trace of *p*-toluenesulfonic acid monohydrate for 0.5 hr at 70°. Removal of volatiles under vacuum gave a brown oil which reluctantly crystallized at −5°. Recrystallization from ethanol gave 3.56 g of tan crystals, mp 110–111°, 42% yield. Norit A treatment in chloroform, followed by two more recrystallizations from ethanol, gave analytically pure, though still tan, **6**, mp 113.5–114.5°.

Anal. Calcd for $C_{15}H_{22}NO_2Cl$: C, 49.52; H, 6.10; N, 3.85; Cl, 9.75. Found: C, 49.79; H, 6.10; N, 3.71; Cl, 9.70.

***N*-Methoxy-2,6-lutidinium Iodide (9).** To our knowledge this compound has not previously been characterized, though the perchlorate has been prepared from $(\mathbf{1})_2 \cdot HClO_4$ and diazomethane.[21]

The iodide crystallizes from a mixture of **1** and methyl iodide that has been kept in the dark at room temperature for 15 min. The melting point of the first precipitate is not increased by recrystallization from ethyl acetate, mp 118.5° dec. *Anal.* Calcd for $C_8H_{12}INO$: C, 36.25; H, 4.56; N, 5.22; I, 47.79. Found: C, 36.53; H, 4.66; N, 5.52; I, 48.07.

The iodide is readily converted to the perchlorate by dissolving it in absolute ethanol, slowly adding a slight excess of 70% perchloric acid, and then chilling the resulting solution. The precipitate is *N*-methoxy-2,6-lutidinium perchlorate, mp 164° (lit.[21] mp 163–164°).

Alkaline Decomposition of Adducts. General. In a typical experiment, an aqueous solution of the adduct is placed within a liquid–liquid extractor; ether is circulated through the solution while an alkaline solution is added to the solution of the adduct *via* a Teflon capillary. After several hours of extraction, the ether layer is removed and dried with anhydrous magnesium sulfate. Evaporation of the ether leaves a residue which then is analyzed for product composition.

Decomposition of Adducts by Aqueous Base. Adduct **5a** was decomposed in dilute aqueous NaOH. Glpc analysis of reaction products showed the absence of **1** and of cyclohexanone, and the presence of 2,6-lutidine, 1-cyclopentenecarboxaldehyde, and adipoin (2-hydroxycyclohexanone) (**7a**). Tlc analysis of the crude 2,4-DNP precipitate from the product mixture confirmed the presence of the two carbonyl-containing products only.[22]

Adduct **5c** was decomposed by aqueous sodium carbonate. 2,6-Lutidine and adipoin (**7a**) dimer were isolated from the reaction mixture. Tlc analysis of the crude 2,4-DNP precipitate from the product mixture confirmed the presence of **7a** and the absence of 1-cyclopentenecarboxaldehyde in the reaction products.

Adduct **3a** was decomposed in dilute aqueous sodium hydroxide. 2,6-Lutidine and phenacyl alcohol (as its 2,4-DNP derivative) were isolated from the product mixture. Tlc analysis of the crude 2,4-DNP precipitate from the product mixture showed that phenacyl alcohol as well as benzaldehyde and formaldehyde had formed in the decomposition of the adduct.

Adipoin Acetate (7b). Commercial **7a** dimer was heated to reform the monomer. The freshly distilled monomer was then immediately acetylated in acetic anhydride–pyridine.[23]

Decomposition of 5c by Pyridine. The acetylated adduct **5c** (1.30 g, 3.57 mmol) was heated at 100° for 0.5 hr with dry pyridine (200 ml, 23.8 mmol). Nmr analysis showed that 59% decomposition had occurred by that time. The mixture was acidified with 3 *N* sulfuric acid and extracted with ether. **7b** was recovered as an oily residue upon evaporation of the ether. The oil showed no impurities by nmr or infrared analysis, and represented a crude yield of 83%. Crystallization from ligroin gave a 62% yield of solid **7b**, mp 38–39° (lit.[23] mp 41–42°). Thin layer chromatography of the filtrate as well as the originally isolated oily product showed only a negligible amount of impurity. The 2,4-DNP melted at 168.5–169.5°, mmp with authentic material, 168.5–170°.

Thermolysis of 3a. The adduct **3a** (0.504 g) was heated in a short-path distillation apparatus at 128° (0.15 Torr), for 100 min. Distillates were collected in a vessel cooled in an acetone–Dry Ice bath. Trituration of the dark residue with ether gave 0.292 g (89% yield) of $\mathbf{1} \cdot HClO_4$ and 0.256 g (78% yield) upon reprecipitation from acetone by adding ether, mp 141.5–143°. This salt was characterized by equivalent weight (226; calcd 224), infrared spectrum similarity to other 1:1 salts of **1**,[24] and by converting it to the 2:1 salt $(\mathbf{1})_2 \cdot HClO_4$, by adding an equivalent amount of **1** to a solution of the 1:1 salt in nitromethane, followed by precipitation upon addition of ether.

Nmr analysis of the liquid in the collection flask suggested that the material was exclusively phenylacetaldehyde (0.072 g, 41% yield) (t, J = 2, 9.5 ppm; d, J = 2, 3.4 ppm; m, 7.0 ppm); 2,4-DNP derivative, mp 121.8–122.6° (lit.[25a] mp 121°).

Thermolysis of 5a. Analytically pure adduct **5a** (1.10 g) was heated under vacuum at 180° (0.04 Torr). Bubbling of the melted material began immediately. Distillables were collected in an acetone–Dry Ice trap over a 1-hr period, during which time the system attained a temperature of 201° (0.10 Torr). Two layers were trapped, an aqueous lower one and a yellow upper one. The residue was a black powder. Total recovery was 97% of the weight of the starting material.

Trituration of the residue with ethanol, followed by addition of excess ether to the resulting solution, only produced an oily precipitate, but slow recrystallization of this precipitate from absolute ethanol gave 0.202 g (34% yield) of $(\mathbf{1})_2 \cdot HClO_4$, mp 186.5–187.5° (authentic material, mp 187–188°).

The oil in the distillate was analyzed by glpc (10% LAC-728 column, temperature programmed over a 60–200° range), showed a minimum of 12 different compounds. By preparative glpc, one major component (6 mg) was identified as cyclohexanone by odor, retention time, infrared, and preparation of its 2,4-DNP derivative, mp 157.5–158.5° (lit.[25b] mp 162°; undepressed mixture melting point; infrared spectrum of product derivative identical with that of authentic material).

Discussion

Formation of 3c. Styrene oxide (**2**) in nitromethane is inert to 2,6-lutidine *N*-oxide (**1**) in the absence of acid. When trifluoroacetic acid is added the epoxide signals (ABX, 3 d of d's, 2.7–3.8 ppm) disappear; a new singlet appears approximately 20 Hz downfield from, and directly at the expense of, the methyl group singlet from **1** (2.78 *vs.* 2.47 ppm). This development is accompanied by development of a doublet of doublets (5.8 ppm) whose signal area is always one-sixth the area of the new singlet. Other new signals are buried by the huge nitromethane signal. Still others, in the aromatic region, integrate to one-half the area of the new singlet. The acid singlet is observed to migrate rapidly from the typical downfield region upfield to the aromatic region.

These data strongly suggest the formation of the adduct **3c**. The ring methyl signal[26] appears downfield from the amine oxide methyl signal due to a greater deshielding by the formal positive charge on the nitrogen of the adduct, in contrast to the methyl signal of the amine oxide, a compound whose nitrogen bears a

(20) 2,4-Lutidine was oxidized to the amine oxide using a general procedure for such oxidations: A. R. Hands and A. R. Katritzky, *J. Chem. Soc.*, 1754 (1958).

(21) See Table I, footnote *a*.

(22) A detailed tabulation of nmr, ir, and uv data, as well as specific techniques for glpc and tlc, appear in the Ph.D. dissertation of William H. Marmer, Temple University, Philadelphia, Pa., 1970.

(23) M. Bergmann and M. Gierth, *Justus Liebigs Ann. Chem.*, **448**, 71 (1926).

(24) See Table I, footnote *b*.

(25) (a) R. L. Shriner, R. C. Fuson, and D. C. Curtin, "The Systematic Interpretation of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 320; (b) p 362.

(26) The term "ring methyl group" is used throughout this report to indicate a methyl group on a pyridine ring.

Table II. Nmr Spectrum of Isolated 2,6-Lut$^+$-O-CH(Ph)$CH_2OHClO_4^-$ (3a)

Shift in CD_3NO_2, ppm	Pattern	Observed coupling (Hz) in CD_3NO_2	Relative area	Assignment
8.34	m (four signals)		1	Heterocyclic ring, para H
7.84	m (three signals)		2	Heterocyclic ring, meta H
7.56	s		5	Phenyl
5.73	d of d	3.2, 7.9	1	Methine
4.62	d of d	7.9, 13.6	1	Methylene
4.19	d of d	3.2, 13.6	1	Methylene
2.80	s		6	Methyl
3.37	s		1	OH

Table III. Nmr Spectrum of Isolated 2,6-Lut$^+$-O-CH(Ph)$CH_2OHBF_4^-$ (3b)

Shift in CD_3NO_2, ppm	Pattern	Coupling, Hz	Relative area	Assignment
8.27	m (four signals)		1	Heterocyclic ring, para H
7.77	m (three signals)		2	Heterocyclic ring, meta H
7.45	s		5	Phenyl
5.68	d of d	3.5, 7.7	1	Methine
4.93	s		1	OH
4.57	d of d	7.7, 13.4	1	Methylene
4.13	d of d	3.5, 13.4	1	Methylene
2.78	s		6	Me

somewhat attenuated positive charge due to some delocalization of the negative charge cloud of oxygen.

The same deshielding effect should cause the new methine signal to absorb downfield from the original methine of the epoxide. For the same reason it is also reasonable to expect the new methylene signals to absorb downfield from the methylene of the epoxide, but upfield from the new methine. This would place the methylene absorption in the region of the nitromethane signal. On first-order analysis, the new methylene–methine signals should exhibit an ABX pattern of three doublets of doublets, as does styrene oxide. The new signal assignable to the methine of the adduct indeed is a doublet of doublets.

Formation and Isolation of 3a and 3b. Although a crystalline trifluoroacetate (**3c**) cannot be isolated, the adduct is obtainable as the crystalline perchlorate (**3a**) or fluoroborate (**3b**). Perchloric acid or fluoroboric acid is introduced anhydrously by using the amine oxide–acid salt. Reaction is initiated upon addition of the epoxide to a solution of the amine oxide–acid salt in nitromethane. Nmr spectral data are shown in Tables II and III.

Formation of Styrene Oxide Adducts with Other Amine Oxides. Both pyridine *N*-oxide and 2-picoline *N*-oxide react with **2** and trifluoracetic acid in nitromethane solution. Although no crystalline adducts have been isolated, the nmr spectra of reaction mixtures demonstrate that these adducts, too, easily form.

Formation and Isolation of 5a and 5b. **1** reacts readily with **4** in nitromethane in the presence of perchloric or fluoroboric acid. The respective adducts **5a** and **5b** are very easily isolated by precipitation upon addition of ether. The perchlorate adduct may also be synthesized using 2,6-dimethyl-d_6-pyridine *N*-oxide, **1**-d_6. This adduct **5a**-d_6 and the undeuterated perchlorate adduct **5a** each may be acetylated using isopropenyl acetate. The acetylated and deuterated compounds were prepared for the mechanistic study of their basic decomposition. Representative nmr spectral data are in Tables IV and V.

Table IV. Nmr Spectrum of Analytically Pure **5a**

Shift in CD_3NO_2, ppm	Pattern	Relative area	Assignment
8.31	m (four signals)	1.0	Para H
7.82	m (three signals)	2.0	Meta H
3.7–4.8	Broad		Methine, CD_2HNO_2
3.03	s	7.1	OH
2.98	s		Methyl
0.83–2.5	Broad	*Ca.* 10	Methylene

Formation and Isolation of Adducts from 4 and other Amine Oxides. Although no crystalline adduct from 2,4-lutidine *N*-oxide **4** and perchloric acid could be obtained, the crystalline acetylated derivative could be isolated after reaction of the crude, viscous initial adduct with isopropenyl acetate. Nmr signals assignable to the ring ortho and para methyl groups of the acetylated adduct appear at 2.87 and 2.63 ppm, respectively, in CD_3NO_2.

Nmr analysis demonstrates that the epoxide also reacts well with 4-picoline *N*-oxide, though no crystalline material has been isolated. In CD_3NO_2, the methyl signal of the amine oxide appears at 2.35 ppm; the methyl signal from the adduct is seen at 2.68 ppm.

Formation and Isolation of an Adduct (8) from 1 and 1,2-Epoxybutane. **1** readily reacts with 1,2-epoxybutane and perchloric acid in nitromethane, but the nmr spectra of starting materials and of the solution during reaction are complicated, due to the asymmetric center and perhaps the lack of complete regiospecificity of the reaction. Precipitation of a crystalline product occurs upon addition of ether to the

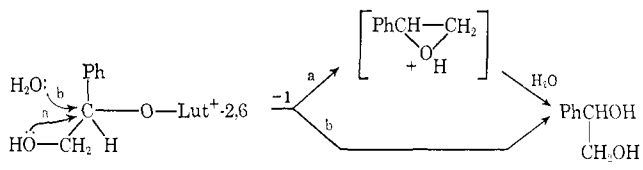
Table V. Nmr Spectrum of **5c**

Shift in CD_3NO_2, ppm	Pattern	Relative area in CD_3NO_2		Assignment
		Cut & weigh	Electronic	
8.45	m (four signals)	1.0	0.8	Para H
8.00	m (three signals)	1.8	2.0	Meta H
4.5–5.5	Broad	2.1	1.7	Methines
3.00	s	6.0	6.0	Methyl
0.83–2.5	Broad			Methylenes
	s	11.6	12.7	$CH_3C(=O)$–

reaction mixture; recrystallization provides a low yield of analytically pure product **8** with a sharp melting point.

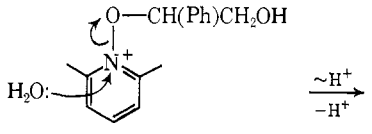
Reactivity of Adducts with Water. All the adducts are stable in water at room temperature overnight. No changes in nmr spectra are observed. With the exception of the styrene oxide adducts, all are also stable to hot (100°) water overnight. The styrene oxide adducts, however, decompose overnight to phenyl-1,2-ethanediol and the amine oxide. Upon heating a D_2O solution overnight, nmr signals assignable to the glycol appear (t, 4.9 ppm, J = 6, methine; d, 3.8 ppm, J = 6, methylene) representing a 63% yield of glycol. The product may result from a displacement reaction at the benzylic carbon (Scheme III).

Scheme III



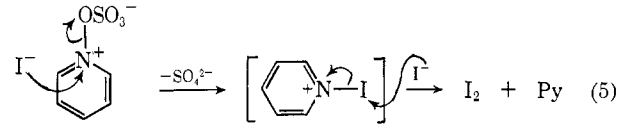
Such mechanisms are reasonable, for substitution at the benzylic position should be facilitated by incipient carbonium ion character in the transition state.

Various *S*-alkoxysulfonium species have been shown to give alcohols by attack by water upon the positively charged sulfur.[27] Analogously, attack upon the positively charged nitrogen in the present adduct would also lead to the observed glycol (eq 4). This is, nevertheless, unlikely; nitrogen bears no low-lying unoccupied orbitals as does sulfur. Furthermore, unlike sulfur in *S*-alkoxysulfonium species, nitrogen in this case is sp^2 hybridized. The failure of water to react with the 1,2-epoxycyclohexane and 1,2-epoxybutane adducts discounts such a mechanism, too. Such attack, however, has been suggested to account for the reaction of iodide ion with pyridine *N*-oxide *O*-sulfonate[28] (eq 5).



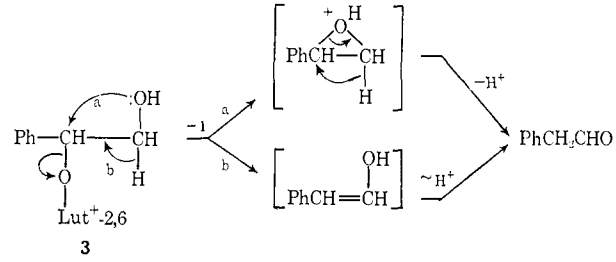
2,6-Lut—O + $HOCH(Ph)CH_2OH$ (4)

Thermolysis of Adducts. Thermolysis of **3** under vacuum produces **1**·$HClO_4$ and $PhCH_2CHO$. It is possible that this reaction proceeds *via* the epoxide,



which then rearranges to the aldehyde by acid catalysis (Scheme IV, path a), or *via* the enol of the aldehyde (Scheme IV, path b).

Scheme IV



Thermolysis of **5a** under vacuum gives a complex mixture of products, among which are the acid and the amine oxide (recovered as (**1**)$_2$·$HClO_4$ upon recrystallization of the residue) and cyclohexanone. The formation of the ketone may be compared to the formation of the aldehyde in the previously discussed thermolysis.

Base-Induced Decomposition of 2,6-Lutidine *N*-Oxide Adducts. In general, the products of base-induced decomposition of the adducts are the same as those identified in the earlier study.[6] The amine oxide oxygen is assumed to become the carbonyl oxygen *via* processes involving proton removal in one of two ways (eq 2 and 3).

Thus, the styrene oxide adducts decompose in pyridine or in alkaline solution to phenacyl alcohol, benzaldehyde, and formaldehyde. The 1,2-epoxycyclohexane adducts, on treatment with alkaline solutions, give **7a** and 1-cyclopentenecarboxaldehyde.

However, the styrene oxide adducts are also quite susceptible to nucleophilic displacement at the benzylic carbon. Nmr data suggest that even the trifluoroacetate anion is capable of displacing the amine oxide group; solutions of the adduct formed by using trifluoroacetic acid slowly undergo transformation into what appears to be CF_3CO_2–$CH(Ph)CH_2OH$, based upon appearance of a signal (t, broad, 6.1 ppm, J = 5.5 in CH_3NO_2) similar to the signal from the benzylic proton of the authentic hydroxytrifluoroacetate.

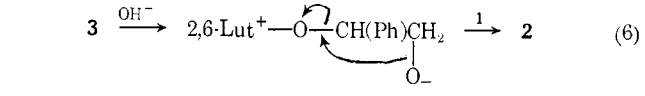
Pyridine seems quite capable of displacing the amine oxide moiety from the styrene oxide adduct in a competitive reaction to the one that gives phenacyl alcohol by the action of pyridine as a base. When **3** or Py^+-O-$CH(OH)CH_2OH$ species each decompose in the presence of pyridine, new nmr signals develop, which

(27) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 5404 (1965).

(28) P. A. S. Smith, H. R. Alul, and R. L. Baumgarten, *ibid.*, **86**, 1139 (1964).

correspond well with the signals from Py^+-CH(Ph)-CH_2OH (3 d of d's in D_2O: 6.4 ppm, J = 5, methine; 4.9 ppm, J = 8, 13, methylene; 4.6 ppm, J = 5, 13, methylene; signal enhancement by addition of authentic material). The formation of the latter compound is documented in the literature.[29]

Aqueous base-induced regeneration of **2** from the styrene oxide adducts is still another example of nucleophilic substitution at the benzylic carbon (proven by nmr and signal enhancement by addition of authentic material) (eq 6).

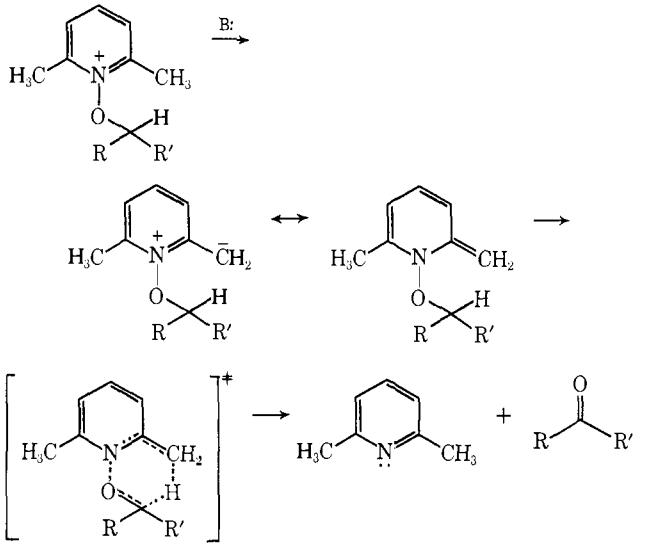


(6)

Thus the basic decomposition of styrene oxide adducts to phenacyl alcohol is overshadowed by several competing reactions, whereas the 1,2-epoxycyclohexane adducts give the α-ketol without any competing reaction other than the carbon–carbon cleavage process that gives 1-cyclopentenecarboxaldehyde.

Mechanism of Base-Induced Decomposition of Adducts from 1. A major goal of this study was to ascertain whether the reaction proceeds as in Scheme V. This is a reasonable proposal; intervention of

Scheme V



the ylide has already been suggested as participating in the decomposition of 1-acetoxy-2-methylpyridinium ions[30] and for $(CH_3)_2S^+$-$OCHR_2$ species.[17] In the present study, deuterium-labeled compounds were examined by nmr spectroscopy during base-induced decomposition.

When 2,6-dimethyl-d_6-pyridine N-oxide, **1**-d_6, is treated with **2** and CF_3CO_2H in CH_3NO_2, **3c**-d_6 is formed. When **3c**-d_6, still in CH_3NO_2 solution with unchanged starting materials, is treated with pyridine, a signal develops in the heterocyclic ring methyl region, at 2.43 ppm. It maximizes at 16% of the theoretical area for completely protonated methyl groups. Since 16% is about one-sixth, superficial interpretation leads to the suggestion that, indeed, the methine proton is transferred to a methyl group of the heterocyclic ring during decomposition to phenacyl alcohol and 2,6-lutidine.

The conclusion that the methine proton in **3c** is transferred to the CH_3 group of lutidine though attractive[31] is equivocal because ylide formation is reversible and the methyl signal of lutidine is superimposable on that of **1**. Therefore, if there is an additional source of exchangeable protons, these protons could find their way to the methyl groups of the adduct before the adduct decomposes. Such exchangeable protons are present in large concentration within the solvent molecules,[32] to a lesser degree on the OH group of the adduct (regardless of the fate of the OH group, this proton remains readily available for exchange), and within the methylene group of the liberated phenacyl alcohol.

To gain meaningful data to substantiate the proposed mechanism,[31] decomposition must be conducted on an *isolated* adduct, the decomposition must proceed *entirely* to the α-ketol, and a way must be found to eliminate the transfer of extraneous protons to the heterocyclic ring methyl groups of the adduct.

By carrying out the decomposition of *isolated* adduct **5c** in aqueous Na_2CO_3 only those products resulting from the process of interest are obtained. Nmr analysis shows that the acetyl group survives the oxidation–reduction process; 2,6-lutidine and **7b** are the initial products; **7b** then undergoes a slower hydrolysis to give **7a** and acetate anion. Tlc of the crude 2,4-dinitrophenylhydrazone–osazone derivatives shows only the DNP and osazone of **7a**, whereas the same technique applied to the decomposition of the nonacetylated adduct also shows the DNP of 1-cyclopentenecarboxaldehyde.

That the ylide forms reversibly during this alkaline decomposition process is demonstrated as follows. When nondeuterated adduct is decomposed in alkaline D_2O, the *isolated* 2,6-lutidine bears a substantial amount of deuterium among its methyl groups, based upon comparison of the integration of 2,6-lutidine's aromatic signals and its methyl signal. Such an exchange must be occurring either upon the adduct and/or upon the liberated 2,6-lutidine. However, when 2,6-lutidine is subjected to the same conditions (actually more severe), no such exchange is detectable by nmr analysis. Thus, exchange must be occurring only on the adduct, through reversible formation of the ylide. This process has been demonstrated for adducts **5a**, **5c**, **6**, **8**, and **9**.

In order to show that adduct decomposition by aqueous base proceeds *via* methine proton transfer to a ring methyl group, and most reasonably by transfer to the carbanion center of the ylide, the acetylated, deuterated adduct **5c**-d_6 is prepared, and then decomposed in Na_2CO_3–D_2O. This time, reversible ylide formation can only yield starting adduct. The 2,6-lutidine isolated from the decomposition reaction is always observed to contain only 1.0 protium per molecule within the methyl groups. Thus, exactly one protium is being transferred to the heterocyclic ring methyl group *during* the step leading to the formation of 2,6-lutidine. Were this process to occur *before*

(29) L. C. King, N. W. Berst, and F. N. Hayes, *J. Amer. Chem. Soc.*, 71, 3498 (1949).

(30) V. J. Traynelis and P. L. Pacini, *ibid.*, 86, 4917 (1964).

(31) W. N. Marmer and D. Swern, *Tetrahedron Lett.*, 531 (1969).

(32) Indeed, when unlabeled adduct is decomposed in pyridine–CD_3NO_2, the CD_2HNO_2 signal enlarges and the ring methyl signal broadens and diminishes, suggesting that exchange between adduct and solvent molecules is significant.

Table VI. Nmr Spectrum of 2,4-DNP of **7b**

Shift in $CDCl_3$, ppm		Pattern	Relative area		Assignment
A[a]	B[b]	A, B	A	B	A, B
11.08	11.13	Broad	0.84	0.8	NH
9.00	9.08	d (J = 2.5)	0.79	1.1	ArH_3
8.27	8.30	d of d (J = 2.5, 10)	1.1	1.0	ArH_5
7.83	7.88	d (J = 10)	1.1	1.0	ArH_6
5.45	5.48	Broad	1.0	0.7	Methine
2.3–3.0	2.3–3.0	Broad	2.4	1.3	Methylene α to C=N
1.5–2.3	1.5–2.3	Broad			Other methylene
2.12	2.13	s	11.4	10.2	Ac

[a] A = values for DNP prepared from **7b** obtained from the decomposition of adduct **5c** in pyridine. [b] B = likewise, from the decomposition of adduct **5c**-d_6 in pyridine.

2,6-lutidine is liberated, the equilibration between adduct and ylide would diminish the 1.0 protium content. Once 2,6-lutidine is liberated, however, no H–D exchange can occur.

There can be little doubt that the process being observed is an intramolecular one. An intermolecular process should be no more favorable than direct methine hydrogen abstraction, whereas rapid ylide formation, followed by internal methine proton transfer through a favorable, six-centered cyclic transition state, is a reasonable alternative to direct methine proton abstraction by aqueous base.[33]

When 2,6-Lut$^+$-d_6-OCH_3I^- (**9**-d_6) is treated with NaOD–D_2O, and the 2,6-lutidine, which is produced together with formaldehyde, is isolated, once again the 2,6-lutidine is found to contain exactly 1.0 protium per molecule within its methyl groups. Furthermore, when 2,6-Lut$^+$-OCD_3I^- is treated with NaOH–H_2O, one deuterium per molecule is detected within the methyl groups of recovered 2,6-lutidine. Therefore, for the general case of *N*-alkoxy-2,6-lutidinium salts, base-induced decomposition proceeds *via* internal proton transfer.

5c is stable in cold pyridine, but when the solution is heated, once again the oxidation–reduction process takes place; no other processes are observed. In this case, the initially formed **7b** is stable and isolable in high yield. (For nmr experiments in which **5c**-d_6 is decomposed in pyridine, pyridine-d_5 is used for convenience.)

Instead of the expected 1.0 proton per molecule within the methyl groups, the isolated 2,6-lutidine consistently bears 1.8 protons. When pyridine is used instead of alkaline D_2O, the major difference is that there no longer is a huge deuterium pool to absorb any exchangeable protium. If a drop of D_2O is added to the pyridine solution prior to decomposition of the adduct, decomposition leads to 2,6-lutidine with only the expected single proton (1.1 H experimentally) per molecule within the methyl groups. Therefore, the extra 0.8 H results from extraneous proton sources, and these sources do not interfere if a deuterium pool is present.

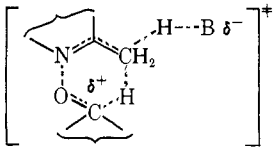
A logical source for this excess protium is water; however, when a cold, and therefore unreactive, solution of the adduct **5c**-d_6 in pyridine is purposely wet with D_2O, then dried with an amount of molecular sieves known to be sufficient to dry the system,[34] and finally heated to induce decomposition, the 2,6-lutidine that is recovered still bears 1.8 protium per molecule within the methyl groups. Clearly, if water were the source of the excess 0.8 H, the methyl protium count now would be significantly less than 1.8 H; even if the system still were wet, it now would be wet with D_2O.

Another potential source of excess protium is **7b**, which has three potentially exchangeable protons upon the carbons α to the carbonyl group. The 1.8 H value actually may be increased significantly by incorporating excess **7b** into the pyridine prior to the addition of this pyridine to the adduct.[35] **7b** may be isolated from a reaction mixture and subjected to nmr analysis. Its 2,4-DNP provides a spectrum in which the acidic protons may be analyzed more easily than is the case with the nonderivatized material. If these acidic protons are the source of the excess 0.8 H found in the liberated 2,6-lutidine, then recovered **7b** should bear 0.8 D. Nmr data in Table VI indeed show that approximately one proton of the three acidic protons of the recovered **7b** is missing.

In conclusion, then, the two *N*-alkoxy-2,6-lutidinium salts that have been studied decompose in base to 2,6-lutidine and a carbonyl compound not by direct abstraction of the α-proton, but by intramolecular α-proton transfer to a heterocyclic ring methyl group, probably by a process involving reversible ylide formation followed by intramolecular α-proton transfer to the carbanion center of the ylide.

Base-Induced Decomposition of a 2,4-Lutidine *N*-Oxide Adduct. Nmr data in Table VII show that the

(33) Analogous to the discussion concerning the E1cB *vs.* E2 mechanisms of elimination by R. Breslow [*Tetrahedron Lett.*, 399 (1964)], a plausible, alternative mechanism of adduct decomposition would be one in which the transition state involves both the adduct and the external base. In this case, the ylide may form but not be a reaction intermediate. Nevertheless, such a transition state requires much higher ordering than the intramolecular one that involves methine proton transfer to the carbanion center of the ylide.



(34) Linde Molecular Sieve Type 4A (0.794 g) is capable of drying a 5.0% D_2O solution in pyridine (1 ml) to 0.10% D_2O within 30 min at room temperature (Karl Fischer aquametric titrations). The pyridine-d_5 originally contained 0.04% H_2O; D_2O was added to it to make a 3.8% D_2O solution in pyridine, which was then dried for 30 min over 2.28 g of type 4A sieves/ml of solution. This should have been sufficient to return the pyridine-d_5 to its original dryness, but containing D_2O rather than H_2O.

(35) When adipoin acetate is present in molar ratios to adduct and to pyridine-d_5 of 1.6:1.0:10, respectively, the 2,6-lutidine that is isolated from the ensuing decomposition contains 1.9 protons per molecule within the methyl groups. This is increased to 2.0 protons per molecule when the initial molar ratios are 4.7:1.0:10, respectively.

Table VII. Nmr Data. Isolated 2,4-Lutidine from Decomposition of **6** in Na_2CO_3–D_2O

Shift in CCl_4, ppm	Pattern	Relative area	Assignment
8.2	d (broad)	0.3	Ortho H
6.8	m	2.0	Meta H's
2.42	s (broad)	1.9	Ortho Me
2.25	s (broad)	2.3	Para Me

2,4-lutidine that is isolated from the decomposed adduct **6** in Na_2CO_3–D_2O contains a substantial amount of deuterium not only within the methyl groups, but also at the ortho position. Ring hydrogens of adducts of 2,6-lutidine *N*-oxide have shown no such propensity toward H–D exchange, but it is not surprising that such exchange is seen in this case. It already has been documented that ortho hydrogens of pyridinium salts undergo such exchange at a rate that is two orders of magnitude greater than the exchange rate of meta hydrogens, and three orders of magnitude greater than the rate of exchange of the para hydrogen.[36–38]

Acknowledgment. The authors thank the U. S. Public Health Service for financial support under research grants CA-7174, CA-7803, and CA-10439 of the National Cancer Institute. The authors also thank Drs. David R. Dalton and John R. Williams for helpful discussions, and the Reilly Tar and Chemical Co. for providing samples of some amines and amine oxides.

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Demonstration of Intermediates in the Hydrolysis of 4-Ethoxypyrylium Salts

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Abstract: The formation of open chain diketone intermediates has been demonstrated during the hydrolysis of 4-ethoxypyrylium salts. Reaction occurs at both $C_{2(6)}$ and C_4 positions to yield open chain diketone and 4-pyrone, respectively; the diketone (a vinyl ether) hydrolyzes and cyclizes to give the 4-pyrone. The yield of 4-pyrone is stoichiometric and oxygen-18 and deuterium isotope experiments show that at low pH the direct mechanism (attack at C_4) predominates but at high pH the diketone intermediate ($C_{2(6)}$ attack) is predominantly involved. The maximal concentration of intermediate varies with pH according to an equation derived from the proposed theoretical mechanism and can be accurately predicted using rate constants reported here. The rate constant for decomposition of pyrylium salt is given by the equation $k_a = k_0 + k_B[B] + k_{OH}[OH^-] + k_{H_3O}/(1 + a_H/K_a)$. The ionization term in the equation can arise from the pH-dependent partitioning of a cyclic hemiacetal intermediate between pyrylium salt and diketone intermediate. Decomposition of the diketone intermediate to give 4-pyrone is specific acid catalyzed (the existence of a preequilibrium protonation is supported by an inverse deuterium isotope effect) and is rate determining at high pH but as the pH decreases the formation of diketone becomes rate determining. However, the latter rate constant decreases with decreasing pH and a pH-independent direct attack of water at C_4 becomes predominant (k_0); the rate constant for 4-pyrone production (k_b) therefore exhibits a plateau region at low pH. The diketone intermediate is shown to yield 2,6-dimethyl-4-pyrone *via* a pathway not including diacetylacetone.

4-Alkoxypyrylium salts were first synthesized over 50 years ago[1] and their lability to water and alcohols is a well-known property.[2,3] However, no mechanistic studies of the hydrolysis reaction have yet been reported. Calculation of the electron density in the pyrylium nucleus indicates that the $C_{2(6)}$ position is favored for nucleophilic addition;[4] however, recrystallization of the 4-methoxypyrylium salt from ethanol yields the 4-ethoxy salt[2] and when treated with water the latter yields the 4-pyrone.[3] Attack of hydroxide and water at C_2 is observed in other pyrylium salts with ring opening.[5]

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Experimental Section

Materials. Oxygen-18 enriched water (1.7% ^{18}O; 0.122% ^{17}O) was obtained from Yeda Research and Development Co. at the Weizmann Institute. 2,6-Dimethyl-4-pyrone was prepared according to Otha and Kato.[6] The pyrone had mp 132–133° (lit.[6] mp 130°); uv max (phosphate buffer, pH 6) 250 nm (ε 15,150). 2,6-Dimethyl-4-ethoxypyrylium tetrafluoroborate was prepared according to Meerwein.[7] The material had mp 90° (lit.[10] mp 90–91°); uv max (phosphate buffer, pH 6), 248 nm (ε 16,700), (CH_3CN), 247 nm (ε 12,000).

4-Pyrone was prepared according to Willstätter and Pummerer[8] by the decarboxylation of chelidonic acid. The product had bp 107–108° (15 mm) (lit.[8] bp 97° (13 mm)); mp 31–33°; uv max (CH_3CN), 243 nm (ε 10,150).

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