ring was continued at 55–60° for 4 hr. The mixture was then cooled to room temperature; precipitated sodium chloride was filtered off and washed with a small amount of tetrahydrofuran. Evaporation of the combined solutions *in vacuo* provided 0.81 g. (98%) of crude Vd as a deep red crystalline solid. After treatment with Darco and recrystallization from 95% ethanol, the yield of colorless Vd, m.p. 172.5–174°, was 0.65 g. (79.5%).

The identity of the product with samples of Vd prepared by methods A and B was substantiated by infrared analysis and a mixed melting point determination.

2,2,4-Tribenzyl-2H,3H-thieno[3,2-b]pyrrol-3-one-1,1-dioxide (IX).—To a solution of 0.41 g. (1.0 mmole) of Vd in 3 ml. of boiling glacial acetic acid was added 0.5 ml. of 30% hydrogen peroxide and the mixture was refluxed for 5 min. After this period, an additional 0.5 ml. of 30% hydrogen peroxide was added and refluxing was continued for 45 min. The colorless solution was then allowed to cool to room temperature over a period of 2 hr. (slow cooling is necessary in order to avoid precipitation of the reaction product as an oil) and finally was refrigerated overnight. The resulting colorless precipitate was filtered, washed with a small amount of ice water, and dried *in vacuo* overnight. The crude sulfone IX, m.p. 155–157°, weighed 0.19 g. (43.0%). Additional product (0.07 g.) was obtained by concentration of the mother liquor under reduced pressure, bringing the total yield to 0.26 g. (59.0%).

An analytical sample of IX was prepared by two recrystallizations from 95% ethanol yielding colorless, glistening needles, m.p. 159–160°.

The infrared spectrum of IX (KBr pellet) showed characteristic bands at 1688 s (C=O), 1494 m and 1454 (aromatic C=C), 1294 s and 1132 s (sulfone), 1080 m, 1073 m, 773 m, 753 m, 740 m, 732 m, 716 s, and 704 s cm.$^{-1}$ (monosubstituted aromatic).

Anal. Calcd. for $C_{27}H_{23}NO_3S$: C, 73.43; H, 5.25; N, 3.18. Found: C, 73.03; H, 5.24; N, 3.11.

2H,3H-Thieno[3,2-b]pyrrol-3-one-1,1-dioxide (X).—A mixture of 1.39 g. (0.01 mole) of I in 8 ml. of glacial acetic acid and 6.6 ml. of 30% hydrogen peroxide was refluxed for 1 hr. and then kept at room temperature for 60 hr. The crystalline product which separated partially was filtered and dried to give 0.60 g. (35.1%) of sulfone X, m.p. 237–239°. The major amount of reaction product (0.92 g., m.p. 228–232°) was obtained upon evaporation of the acetic acid solution *in vacuo;* total yield 88.8%. A sample recrystallized twice from 95% ethanol afforded colorless needles, m.p. 239–241°. The infrared spectrum of X (Nujol/HCBD) showed characteristic bands at 3240 m (N—H), 1693 s (C=O), 1307 s and 1126 s cm.$^{-1}$ (sulfone).

Anal. Calcd. for $C_6H_5NO_3S$: C, 42.09; H, 2.95; N, 8.18. Found: C, 41.76; H, 2.86; N, 8.07.

2-Benzylidene-2H,3H-thieno[3,2-b]pyrrol-3-one-1,1-dioxide (XI).—To a solution of 1.0 g. (4.4 mmoles) of benzylidene compound VI in 6 ml. of boiling glacial acetic acid was added 1 ml. of 30% hydrogen peroxide. After refluxing for 5 min., an additional 1 ml. of 30% hydrogen peroxide was added, and refluxing was continued for another 30 min. until the color of the solution had changed to light yellow. The reaction mixture was allowed to cool to room temperature and the resulting colorless precipitate was filtered, washed with 15 ml. of water, and dried overnight. The crude sulfone XI, m.p. 233–234°, weighed 0.84 g. (73.7%). An additional 0.13 g. of XI could be obtained by addition of water to the mother liquor, bringing the total yield to 0.97 g. (85%). Two recrystallizations from 95% ethanol afforded colorless needles, m.p. 236–238°.

The infrared spectrum of XI (Nujol/HCBD) showed bands at 3160 m (N—H), 1682 s and 1666 s (C=O), 1308 s and 1142 s cm.$^{-1}$ (sulfone); other major absorptions at 1598 s, 1455 m, 1158 m, 1082 m, 1059 m, 777 s, 736 m, and 682 m cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_9NO_3S$: C, 60.21; H, 3.50; N, 5.41. Found: C, 60.46; H, 3.60; N, 5.45.

Cleavage of Alkyl o-Hydroxyphenyl Ethers

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A facile cleavage of the vanillin methoxyl group has been discovered and the reaction has been successfully extended to a number of other alkyl o-hydroxyphenyl ethers.

The ready availability of vanillin from lignin has prompted a study of various reactions which could conceivably lead to greater utilization of this material. Foremost among the reactions under study was demethylation, for a facile cleavage of the vanillin methoxyl group would provide a good route to protocatechualdehyde, which is an intermediate with interesting possibilities. A cheap, efficient reaction of this type has been singularly lacking.

The demethylation of vanillin has been effected by the use of dilute hydrochloric acid,[1] by 48%

hydrobromic acid in glacial acetic acid,[2] and by phosphorus pentachloride,[3] but the yields were less than 50%. These results were confirmed in the present investigation.

The stability of the vanillin or isovanillin (3-hydroxy-4-methoxybenzaldehyde) structures toward the usual demethylating conditions is illustrated by the behavior of veratraldehyde toward diverse reagents; treatment with boiling 43% hydrobromic acid for three hours gave a 27% yield of isovanillin,[4] while heating at 60° for six hours with anhydrous aluminum chloride and benzene afforded vanillin in 67% yield.[5] Apparently,

(1) F. Tiemann and W. Haarmann, *Ber.*, 7, 608 (1874).

(2) R. Stoermer, *Ber.*, 41, 321 (1908).

(3) K. Freudenberg and W. Heel, *Chem. Ber.*, 86, 190(1953).

(4) A. Lovecy, R. Robinson, and S. Sugasawa, *J. Chem. Soc.*, 817 (1930).

(5) H. E. Ungnade and E. W. Crandall, *J. Am. Chem. Soc.*, 71, 2209 (1949).

little, if any, protocatechualdehyde was formed in either case. An interesting sidelight to these results is the fact that in similar structures there is additional evidence for selective demethylation at either the *meta* or the *para* position relative to the carbonyl.[6,7]

The first report of a satisfactory demethylation of vanillin from the yield standpoint came from Pearl and Beyer,[8] who obtained 93% of crude protocatechualdehyde by reaction of vanillin with anhydrous aluminum bromide in nitrobenzene at 95°. Recently, a variation[9] of this procedure was used to obtain a similar yield.

In the present investigation, repetition of some of the aforementioned literature references and trials with other conventional reagents such as amine hydrohalides and anhydrous zinc chloride were all unsuccessful. However, further investigation has revealed a novel method of demethylating vanillin which combines the features of simplicity, moderate cost, high yield, and exceptional purity of product. Thus, anhydrous aluminum chloride in the presence of pyridine effects the demethylation of vanillin in 85–90% yield by refluxing in methylene chloride solution at 45° for twenty-four hours. The preferred molar ratios of reactants are 4.4:1.1:1.0 pyridine–aluminum chloride–vanillin. Furthermore, when the reaction was extended to other ethers, it was found that the reagent appears to be quite selective in that neighboring group participation of the *ortho* hydroxyl is involved. Thus, such representative alkyl aryl ethers as anisole, *m*-methoxybenzaldehyde, resorcinol monomethyl ether, veratraldehyde, and piperonal were essentially unaffected by the conditions of the reaction, while all alkyl *o*-hydroxyphenyl ethers which were tried, with the single exception of *o*-vanillin (2-hydroxy-3-methoxybenzaldehyde), were successfully cleaved (see Table I). Attempts to use, with pyridine, other Lewis acid catalysts such as boron trifluoride, ferric chloride, and zinc chloride instead of aluminum chloride in the demethylation of vanillin met with no success whatever. At the most, only trace amounts of protocatechualdehyde were obtained. An interesting effect was observed when pyridine was replaced by various other tertiary amines in the demethylation of vanillin. No other amine gave as good results as pyridine for what were apparently largely steric reasons; 4-methylpyridine gave better results, by far, than 2- or 2,5-substituted derivatives (see Table II).

A number of solvents were tried for the demethylation of vanillin and nonpolar solvents such as benzene and carbon tetrachloride failed to dissolve the reaction complex. However, polar halo-

(6) I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **74**, 4262 (1952).

(7) M. Allen, A. L. Promislow, and R. Y. Moir, *J. Org. Chem.*, **26**, 2906 (1961).

(8) I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **75**, 2630 (1953).

(9) J. Kamlet, U. S. Patent 2,975,214, March 14, 1961.

TABLE I
CLEAVAGE OF ALKYL *o*-HYDROXYPHENYL ETHERS

Ether	Product[a]	M.P.[b]	Yield, %[c]
Vanillin	Protocatechualdehyde	153–154	86.8
Isovanillin	Protocatechualdehyde	153–154	88.0
Acetovanillone	3,4-Dihydroxyacetophenone	110–112	70.0
Vanillic acid	Protocatechuic acid	[d]	28.5
Guaiacol	Catechol	103–105	73.6
3-Ethoxy-4-hydroxybenzaldehyde	Protocatechualdehyde	[e]	32.0
Syringaldehyde	3,4-Dihydroxy-5-methoxybenzaldehyde[f]	131–133.5	78.5
5-Bromovanillin	5-Bromoprotocatechualdehyde	225–227	95.1

[a] Products were identified by melting point and mixture melting point with authentic samples except as noted. [b] Melting points were determined in a capillary tube on the solid product left from the evaporation of ether without further purification and are uncorrected. [c] Yield figures are based on amounts of product actually isolated except as noted. The data are from unreplicated experiments in each case except for vanillin and 3-ethoxy-4-hydroxybenzaldehyde; in the latter case, the reaction time was doubled to give improvement from 14% to the figure shown. [d] Demethylation was incomplete because of poor solubility of the reaction complex in methylene chloride. The product was a mixture of protocatechuic and vanillic acids which was subjected to infrared analysis to determine the yield. [e] Infrared analysis was used on the product which was a mixture of 3-ethoxy-4-hydroxybenzaldehyde and protocatechualdehyde. [f] The normal amounts of reagents for cleaving a single methoxyl were used.

genated alkanes in general were very effective and the polarity apparently had some effect on the extent of demethylation. When chloroform or ethylene chloride, each of which has about the same polarity, was used as solvent the yields were about 75%. Use of the more polar methylene chloride or ethyl bromide gave 87% protocatechualdehyde. The reaction is visualized as proceeding through a solvated, five-membered cyclic intermediate I, which is attacked by pyridine in a nucleophilic displacement reaction resulting in the formation of II, which yields protocatechualdehyde on hydrolysis. On the basis of this mechanism, the failure of *o*-vanillin to undergo cleavage could be explained by the fact that, of the two groups

TABLE II
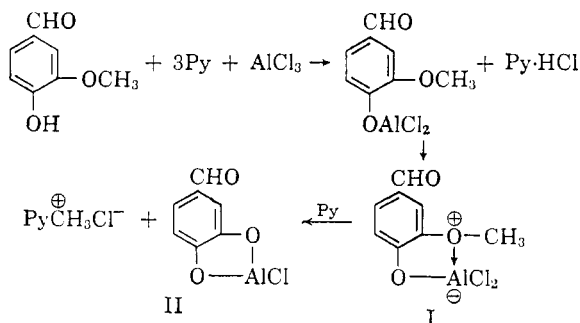### DEMETHYLATION OF VANILLIN WITH ANHYDROUS ALUMINUM CHLORIDE AND VARIOUS TERTIARY AMINES

Tertiary Amine	% Yield of Protocatechualdehyde
2-Methylpyridine	41.3
2-Methyl-5-ethylpyridine	36.7
4-Methylpyridine	72.7
Quinoline	22.6
Dimethylaniline	33.1
Triethylamine	61.5

adjacent to the hydroxyl, the carbonyl oxygen is more basic than the methoxyl oxygen, which would tend to give an aluminum complex involving the carbonyl rather than the methoxyl. In the case

of 3-ethoxy-4-hydroxybenzaldehyde, cleavage of the ethoxyl group was undoubtedly inhibited by steric hindrance and the inductive effect of the electron-releasing methyl group which tends to repel a nucleophilic reagent. This effect has been noted previously in a study of the alkaline hydrolysis of alkyl bromides.[10]

Experimental

The reactions of alkyl o-hydroxyphenyl ethers with anhydrous aluminum chloride and pyridine were carried out according to a standardized procedure which is given in detail for vanillin.

Protocatechualdehyde.—Anhydrous aluminum chloride (9.7 g., 0.0724 mole) was suspended in a solution of 10 g. (0.0658 mole) of vanillin in 100 ml. of methylene chloride in an apparatus protected from atmospheric moisture. While stirring briskly and cooling to maintain the temperature at

30–35°, 22.9 g. (0.290 mole) of pyridine was added slowly. The reaction was vigorous; the resulting clear, light orange solution of the reaction complex was heated to reflux (45°) and maintained at that temperature while stirring for 24 hr. The solution, which had darkened only slightly during the reflux period, was cooled to 25° and the product was hydrolyzed, while stirring and maintaining the temperature at 25–30°, by the addition of dilute (15–20%) hydrochloric acid until the mixture was definitely acidic to Congo Red indicator. Of the two phases present at this time, the lower methylene chloride layer contained most of the small amount of unchanged vanillin and essentially no protocatechualdehyde; the latter was dissolved in the aqueous phase. Evaporation of the methylene chloride solution yielded 0.8 g. of vanillin. Extraction of the aqueous phase with ether followed by evaporation of the ether left 7.9 g. (87%) of pale yellow crystals of protocatechualdehyde melting at 153–154°.

Essentially equivalent results were obtained by an alternative procedure whereby the pyridine was added with cooling and stirring to the aluminum chloride slurried in pentane resulting in the formation of an aluminum chloride-pyridine complex, presumably that containing 3 moles of pyridine per mole of aluminum chloride.[11] Evaporation of the pentane left a white crystalline solid containing unreacted pyridine which was added to the solution of vanillin in methylene chloride and the reaction was carried on as in the first instance. The first technique, because of its convenience, is the method of choice.

The alkyl o-hydroxyphenyl ether must be either added to the aluminum chloride while dissolved in the halogenated alkane solvent or it must be mixed intimately with the aluminum chloride before the solvent is added in order to prevent reaction of the solvent with the metal chloride. A similar protection of halogenated alkane solvents in the presence of anhydrous aluminum chloride has been observed previously.[12]

(10) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

(11) R. E. Van Dyke and H. E. Crawford, *J. Am. Chem. Soc.*, **73**, 2022 (1951).

(12) M. S. Carpenter and E. C. Kunz, U. S. Patent 2,027,148 January 7, 1936.