It might also be noted that the data, within experimental error, extrapolates to zero rate in the absence of ethylene, thus suggesting that hydrogen bromide does not promote aluminum bromide in the absence of trace quantities of olefin.

In summary, a co-catalyst seems to play a dual role in Friedel–Crafts catalysis in both increasing the number of chain carriers and in facilitating bimolecular chain stopping reactions.

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Reactions of α-Hydroxy Ketones with Ammonia[1,2a]

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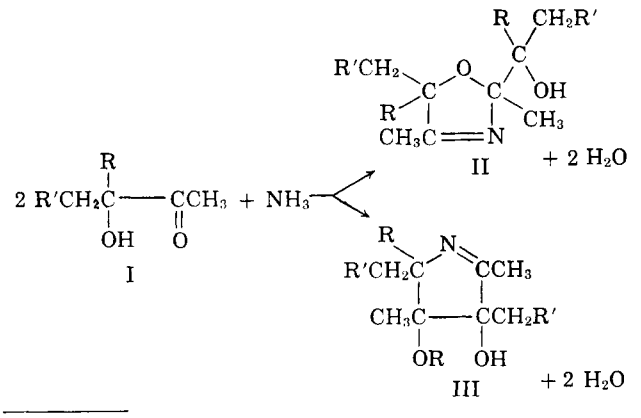
α-Hydroxy ketones react with ammonia to yield 3-oxazolines and 3,4-dihydro-2*H*-pyrrolenine-3,4-diols. The structure of the α-hydroxy ketone determines which of the two isomeric heterocyclic compounds will be formed. The 3-oxazoline structure represents a new series of heterocyclic compounds.

In 1956, Asinger and Thiel[3] published the first of a series of articles on the concomitant reactions of ketones, ammonia, and sulfur. Their reactions led primarily to the formation of 3-thiazolines. They proposed a mechanism whereby an α-mercapto ketone is formed as an intermediate.[4] In later work[5] this proposed intermediate was shown to be correct, as α-mercapto carbonyl compounds condensed with carbonyl compounds to form 3-thiazolines. Their reactions were extended to cover the formation of *m*-thiazines from β-mercapto ketones.[6]

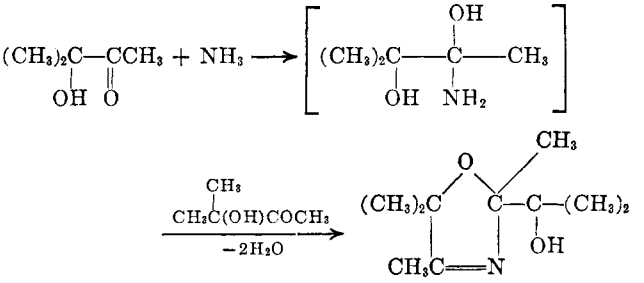
The analogy to hydroxy ketones is apparent, and research was conducted on the possibility of forming 3-oxazolines from a reaction of α-hydroxy ketones with ammonia and carbonyl compounds. The reactions, however, proved to be more complex than those of the sulfur analogs, due primarily to the high reactivity of α-hydroxy ketones with nucleophilic reagents.[7]

The general reaction of α-hydroxy ketones with ammonia is illustrated.

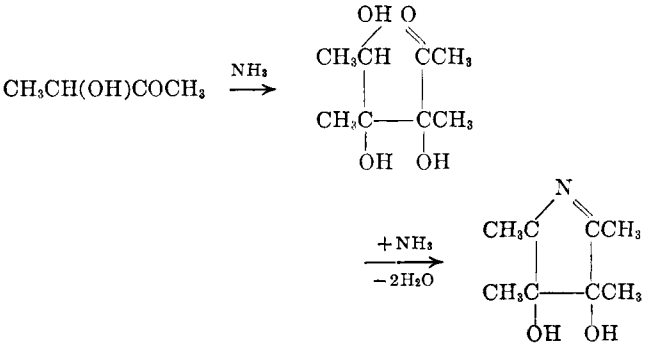


In this reaction R must be alkyl for the formation of II, and for III it must be hydrogen; R′ can be either alkyl or hydrogen.

The mechanism proposed for the formation of II is exemplified by the formation of 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline (II, R = CH_3, R′ = H) from the reaction of 3-hydroxy-3-methyl-2-butanone with ammonia.



If R in formula I is hydrogen, the reaction apparently proceeds through an aldol condensation and final condensation of the γ-hydroxy ketone to form the isomeric 3,4-dihydro-2-*H*-pyrrolenine-3,4-diol.



The third possibility, an α-hydroxy ketone holding two α-hydrogen atoms on the hydroxy-carbon atom, should theoretically lead to pyrroleninediols. With acetol, however, extensive polymerization precluded any isolable product.

The 3-oxazolines represent a new series of heterocyclic compounds, as the only reported 3-oxazolines are actually the enolic ethers of the corresponding 4-

(1) The authors are indebted to The Petroleum Research Fund (PRF grant #685-A) for the support of the work reported in this paper.

(2) (a) Taken from the M.S. thesis of D.D.L., South Dakota School of Mines and Technology, 1962. (b) Present address, Eastman Kodak Company, Rochester, N. Y.

(3) F. Asinger, *Angew. Chem.*, **68**, 413 (1956).

(4) F. Asinger, M. Thiel, and E. Pallas, *Ann.*, **602**, 37 (1957).

(5) F. Asinger, M. Thiel, and G. Esser, *ibid.*, **610**, 33 (1957); M. Thiel, F. Asinger, and K. Schmiedel, *ibid.*, **611**, 121 (1958).

(6) F. Asinger, M. Thiel, and W. Horingklee, *ibid.*, **610**, 1 (1957); M. Thiel and F. Asinger, *ibid.*, **610**, 17 (1957).

(7) The reaction rate constant for the reduction of 3-hydroxy-2-butanone with sodium borohydride is equivalent to that of propionaldehyde: E. H. Jensen, "Sodium Borohydride—Potassium Borohydride," R. C. Wade, ed., Metal Hydrides, Inc., 1958, p. 19.

oxazolidinones.[8] Bergmann, *et al.*,[9] have established infrared absorption bands for the O–C–N system in oxazolidines; the O–C–N system has three bands (at 1149–1185, 1116–1139, and 1086–1114 cm.$^{-1}$, respectively) in the 1100–1200-cm.$^{-1}$ region. The absorption of the aliphatic C=N double bond is well known,[9] lying at about 1670 cm.$^{-1}$.

The infrared spectra of the compounds are summarized in Table I. Acid hydrolysis of the 3-oxazoline structure should yield the original α-hydroxy ketone and an ammonium salt. This was shown to be true; an example is given in Experimental.

TABLE I

INFRARED SPECTRA

Compound	Significant infrared bands (cm.$^{-1}$)[a] O—C—N	C=N	OH[b]
2-(1-Hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline	1156, 1122, 1069	1652	3550
5-Ethyl-2-(1-hydroxyl-1-methylpropyl)-2,4,5-trimethyl-3-oxazoline	1150, 1123, 1079	1668	3580
2-(1,3-Dimethyl-1-hydroxybutyl)-5-isobutyl-2,4,5-trimethyl-3-oxazoline	1154, 1131, 1099	1660	3560
2,3,4,5-Tetramethyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol		1660	3560
2,4-Dimethyl-3,5-dipropyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol		1656	3540

[a] All infrared spectra were obtained as 5–10% solutions in chloroform using a Perkin–Elmer Infracord, Model 137B. [b] Nonhydrogen bonded OH.

Several 3,4-dihydro-2*H*-pyrrolenines (Δ^1-pyrrolines) have been reported.[10,11] Evans[10] reported the formation of 2,5-dimethyl-3,4-dihydro-2*H*-pyrrolenine from the reaction of γ-chlorovaleronitrile with methylmagnesium iodide. The infrared spectrum of this pyrrolenine is remarkably similar to that of the two pyrroleninediols (with the exception of the OH absorption). The pyrroleninediols are easily oxidized by periodic acid, indicative of the 1,2-diol structure present in these compounds. The pyrroleninediols decompose on standing, whereas the oxazolines show only slight decomposition after a period of nearly one year. Murray and Clark[11] indicated that their Δ^1-pyrrolines completely decomposed after standing in a desiccator for six months.

The α-hydroxy ketones containing an α-hydrogen atom on the hydroxy carbon atom could theoretically form either product II or III. A simple thermodynamic calculation from bond energies[12] indicates that the reaction forming the pyrroleninediol should predominate.

$$CH_3CHOHCOCH_3 + NH_3 \longrightarrow C_8H_{15}O_2N + 2H_2O \quad \Delta H = +0.4 \text{ kcal.}$$

3,4-dihydro-2*H*-pyrrolenine

$$CH_3CHOHCOCH_3 + NH_3 \longrightarrow C_8H_{15}O_2N + 2H_2O \quad \Delta H = +11.9 \text{ kcal.}$$

3-oxazoline

The relatively high, positive ΔH value calculated for the formation of the isomeric 3-oxazoline would account for the lack of its formation in those cases where competition is possible. This thermodynamic data is in agreement with the experimental results as the pyrroleninediols are formed at low temperatures, whereas the oxazolines require comparatively drastic conditions.

Experimental[13]

α-Hydroxy Ketones.—Acetoin was purchased commercially as an 85% aqueous solution and was used without further purification. 3-Hydroxy-3-methyl-2-butanone, 3-hydroxy-3-methyl-2-pentanone, and 3-hydroxy-2-hexanone were prepared from the corresponding acetylenic alcohols (available commercially) by a modified procedure of a British patent,[14] as given below for the butanone. For the preparations of 3-hydroxy-2-methyl-2-pentanone and 3-hydroxy-2-hexanone, it was necessary to use a much smaller scale, as these reactions were even more violent than the reaction forming the butanone. The yields from this method ranged from 70 to 85%. The physical constants obtained for the three ketones were: 3-hydroxy-3-methyl-2-butanone, b.p. 78–79° (100 mm.), n^{30}D 1.412; 3-hydroxy-3-methyl-2-pentanone, b.p. 58–59° (24 mm.), n^{25}D 1.422; 3-hydroxy-2-hexanone, b.p. 163–164° (760 mm.), n^{25}D 1.423. These values correspond well to the literature values.[15,16] As the boiling points of the hydroxy ketones are close to those of the corresponding acetylenic alcohols, infrared spectra were utilized to ascertain the purity of these starting compounds. 3,5-Dimethyl-3-hydroxy-2-hexanone was prepared according to the procedure of Hennion and Watson.[15]

3-Hydroxy-3-methyl-2-butanone.—In a 12-l., three-necked flask equipped with a mechanical stirrer, two efficient reflux condensers, and a thermometer, were placed 120 g. of mercuric sulfate, 3640 ml. of 25% (by weight) sulfuric acid, 1580 ml. of water and 1000 g. of ice. The solution was stirred until the temperature dropped to 10°. 2-Methyl-3-butyn-2-ol, 1395 ml., was gradually added with stirring through one of the reflux condensers. The addition was made at such a rate that the temperature remained below 15°. The mixture was then heated, with rapid stirring, until the very vigorous and exothermic reaction ensued (occurring at approximately 50°). This sudden reaction immediately raised the temperature of the contents of the flask to 98°. After the initial reaction had subsided, the mixture was gently refluxed for a period of 1 hr. Steam distillation, salting with ammonium sulfate, azeotropic distillation with benzene, and fractionation were used successively for isolation of the hydroxy ketone.

2-(1-Hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline.—A pressure reaction apparatus (Paar Series 4500, medium-pressure, stirrer type, 1000-ml. capacity) was charged with 154.4 g. of 3-hydroxy-3-methyl-2-butanone. Anhydrous ammonia was introduced, with stirring, until a pressure of 105 p.s.i.g. was obtained. The bomb was heated to 125° (pressure at 325 p.s.i.g.) and this temperature was maintained for 3.5 hr. Following the removal of ammonia and water, fractionation of the residue at reduced pressure yielded 48.1 g. of recovered hydroxy ketone and 93.8 g. of the oxazoline. The yield based on unchanged ketone was 97%, b.p. 84–85° (5 mm.), m.p. (large, colorless triclinic crystals from ethyl ether) 78°.

Anal. Calcd. for $C_{10}H_{19}O_2N$: C, 64.80; H, 10.33; N, 7.5. Found: C, 64.99; H, 10.21; N, 7.6.

5-Ethyl-2-(1-hydroxy-1-methylpropyl)-2,4,5-trimethyl-3-oxazoline.—The procedure used was the same as that used for the

(8) H. O. L. Fischer, G. Dangschat, and H. Stettiner, *Ber.*, **65B**, 1032 (1932), reported the reaction of 4-oxazolidinones with methyl iodide–silver oxide to yield the 3-oxazolines.

(9) E. D. Bergmann, E. Zimkin, and S. Pinchas, *Rec. trav. chim.*, **71**, 180 (1952).

(10) G. G. Evans, *J. Am. Chem. Soc.*, **73**, 6230 (1951); Evans also prepared the pyrrolenine from 5-chloro-2-hexanone and ammonia.

(11) J. V. Murray and J. B. Clark, *ibid.*, **68**, 126 (1946).

(12) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, New York, N. Y., 1940, pp. 53, 131. The assumptions which Pauling discusses in reference to bond energies must be kept in mind. However, the calculated values of ΔH certainly indicate the order of magnitude.

(13) All melting points are uncorrected.

(14) British Patent 640,477 (July 19, 1950); *Chem. Abstr.*, **45**, 1622h (1950).

(15) G. F. Hennion and E. J. Watson, *J. Org. Chem.*, **23**, 656 (1958). Hennion and Watson reported the following physical constants: 3-hydroxy-3-methyl-2-butanone, b.p. 46–47° (21 mm.), n^{25}D 1.4129; 3-hydroxy-3-methyl-2-pentanone, b.p. 54–56° (21 mm.), n^{25}D 1.4198; 3,5-dimethyl-3-hydroxy-2-hexanone, b.p. 69–70° (17 mm.), n^{25}D 1.4260.

(16) J. Jadot and N. Doyer, *Bull. soc. roy. sci. Liege*, **24**, 2 (1955), reported the boiling point of 3-hydroxy-2-hexanone as 163–165°.

preparation of the 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline with the exception that a higher temperature (150–180°) was necessary for the reaction to occur. The oxazoline was a colorless, viscous liquid with an odor characteristic of all of the oxazolines. The yield was 82% based on unchanged ketone, b.p. 93–94° (2.5 mm.), $n^{20}D$ 1.4593, d_4^{20} 0.955.

Anal. Calcd. for $C_{12}H_{23}O_2N$: C, 67.56; H, 10.87; N, 6.6; MR, 61.60. Found: C, 67.48; H, 10.76; N, 6.7; MR, 61.54.

2-(1,3-Dimethyl-1-hydroxybutyl)-5-isobutyl-2,4,5-trimethyl-3-oxazoline.[17]—This oxazoline was prepared using the conditions that were employed for 5-ethyl-2-(1-hydroxy-1-methylpropyl)-2,4,5-trimethyl-3-oxazoline. A reaction period for 9 hr. gave a quantitative yield,[18] b.p. 90–91° (0.37 mm.), $n^{20}D$ 1.4626, d_4^{20} 0.917.

Anal. Calcd. for $C_{16}H_{31}O_2N$: C, 71.33; H, 11.60; N, 5.2; MR, 80.85. Found: C, 71.12; H, 11.45; N, 5.0; MR, 80.08.

2,3,4,5-Tetramethyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol.—The pressure reaction apparatus[19] was charged with 50 g. of an 85% aqueous solution of 3-hydroxy-2-butanone and 180 ml. of absolute alcohol. Anhydrous ammonia was introduced until a pressure of 100 p.s.i.g. was obtained. During the addition of ammonia the temperature rose from 22° to 50° (probably due to the heat of solution), then slowly dropped to room temperature. The pressure was maintained at 80–100 p.s.i.g. for 2.5 hr. by an occasional addition of ammonia. Following the removal of ammonia, ethanol and water, the residue was fractionated at reduced pressure,[20] yielding 34.2 g. (90.2%) of a light amber-colored, viscous liquid, b.p. 78–80° (6 mm.), $n^{20}D$ 1.4574, d_4^{20} 0.997.

Anal. Calcd. for $C_8H_{15}O_2N$: C, 61.13; H, 9.62; N, 8.9; MR, 43.12. Found: C, 60.63; H, 9.72; N, 9.0; MR, 42.87.

2,4-Dimethyl-3,5-dipropyl-3,4-dihydro-2*H*-pyrrolenine-3,4-diol.—The pressure reaction apparatus was charged with 50.6 g. of 3-hydroxy-2-hexanone and 100 ml. of 95% ethanol. The stirrer was started and anhydrous ammonia was introduced until a pressure of 100 p.s.i.g. was obtained. The pressure was maintained between 75 and 100 p.s.i.g. for approximately 9 hr. Fractionation of the reaction product yielded 42.3 g. of the pyrrolenine (91%), b.p. 94–95° (1.0 mm.), $n^{20}D$ 1.4646, d_4^{20} 0.957.

Anal. Calcd. for $C_{12}H_{23}O_2N$: C, 67.56; H, 10.87; N, 6.6; MR, 61.60. Found: C, 67.67; H, 10.72; N, 6.6; MR, 61.20.

Acid hydrolysis of 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline.—A 50.0-g. sample of 2-(1-hydroxyisopropyl)-2,4,5,5-tetramethyl-3-oxazoline was dissolved in 182 g. of 10% hydrochloric acid, and the solution was refluxed for 23 hr. The reaction mixture was steam distilled, and the distillate was salted with ammonium sulfate. The upper layer from the salting was azeotropically distilled with benzene to remove the water, and the benzene solution was fractionated to yield 50.6 g. (92%) of 3-hydroxy-3-methyl-2-butanone. The residue from the steam distillation was filtered, decolorized with Norite and evaporated to yield 12.2 g. (82%) of ammonium chloride.

(17) The authors are indebted to Mr. Gary R. Hansen for the work on this reaction and most of the micro carbon and hydrogen analyses.

(18) The yield of oxazoline was found to be dependent on the reaction time. An 8–10-hr. period gave rise to essentially quantitative yields in all three cases.

(19) Pressures above atmospheric pressure were not necessary for the formation of the pyrrolenines; however, the reactions were extremely slow.

(20) If the pot temperature during distillation was allowed to rise above 100° (approximately), complete polymerization occurred.

The Preparation of and Equilibrium between Substituted α-Phenyl-*cis*- and *trans*-cinnamic Acids

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The amine-catalyzed Perkin condensations of a series of *p*-substituted phenylacetic acids and benzaldehydes are described. In every case, both *cis* and *trans* isomeric products have been characterized. Substitution of pyridine for triethylamine in condensations with *p*-nitrophenylacetic acids has resulted in increased yields. The equilibrium constant for each pair of isomers has been determined.

The amine-catalyzed Perkin condensation of phenylacetic acids with benzaldehydes[1,2] and the Oglialoro modification[3,4] in which the amine and the acid are replaced by a salt of the acid, both afford α-phenyl-*trans*-cinnamic acids. A minor product is often the isomeric *cis* acid[1-4] but in about half of the condensations reported none of the *cis* acid has been obtained.

Although we were primarily interested in the *trans* acids as intermediates for the synthesis of *cis*-stilbenes, there are several reasons for wanting samples of the *cis* isomers. First, the isolation and spectroscopic study of both isomers provides more direct evidence for the stereochemistry of the products. Second, the system offers interesting possibilities for studying the effect that substituents on the two different rings have on the relative rates of formation of the acids, on the equilibrium between the *cis* and *trans* isomers and upon their acidities. Finally, in view of the known antibacterial and antifungal activity of cinnamic acids,[5] it was of interest to have these properties evaluated in the *cis*- as well as the α-phenyl-*trans*-cinnamic acids.

The condensation of benzaldehyde, anisaldehyde and *p*-nitrobenzaldehyde with each of three similarly *p*-substituted phenylacetic acids has been studied. The data on the preparation of these nine pairs of *cis* and *trans* isomers are summarized in Table I. It was found that the *trans* isomer in each pair was as expected the

(1) (a) L. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., p. 182; (b) J. R. Johnson, *Org. Reactions*, **1**, 225 (1942). Reference 1a names these as *cis*- or *trans*-α-phenylcinnamic acids where the prefixes *cis* and *trans* refer to the relationship between the two phenyl groups, whereas ref. 6 names them as α-phenyl-*cis*- or *trans*-cinnamic acids in which the prefixes refer to the relationship between the carboxylic acid function and the β-phenyl group—*i.e.*, the cinnamic acid moiety. The latter nomenclature is used throughout this report.

(2) (a) R. E. Buckles, M. P. Bellis, and W. D. Coder, Jr., *J. Am. Chem. Soc.*, **73**, 4972 (1951); (b) R. E. Buckles and E. A. Hausman, *ibid.*, **70**, 415 (1948); (c) R. E. Buckles, E. A. Hausman, and N. G. Wheeler, *ibid.*, **72**, 2494; (1950); (d) R. Stoermer and L. Prigge, *Ann.*, **409**, 20 (1915).

(3) (a) H. Lettré and O. Linsert, German Patent 840,091 (May 26, 1952); (b) D. Papa, E. Klingsberg, and E. Schwenk, U. S. Patent 2,606,922 (December 3, 1949); (c) O. Linsert and H. Lettré, U. S. Patent 2,691,039 (April 11, 1951); (d) British Patent 559,024 (August 31, 1942).

(4) (a) M. Bakunin, *Gazz. chim. ital.*, **25**, 137 (1895); (b) D. Papa, H. Breiger, E. Schwenk, and V. Peterson, *J. Am. Chem. Soc.*, **72**, 4906 (1950); (c) B. B. Dey and U. Ramanathan, *Proc. Natl. Inst. Sci., India*, **9**, 193 (1943); (d) V. M. Fedosova and O. Yu. Magidson, *J. Gen. Chem., USSR*, **24**, 701 (1954); (e) M. Crawford and G. W. Moore, *J. Chem. Soc.*, 3445 (1955); (f) T. R. Lewis, M. G. Pratt, E. D. Homiller, B. F. Tullar, and S. Archer, *J. Am. Chem. Soc.*, **71**, 3749 (1949); (g) E. Schwenk, D. Papa, B. Whitman, and H. F. Ginsberg, *J. Org. Chem.*, **9**, 175 (1944).

(5) I. A. Pearl and D. L. Beyer, *ibid.*, **16**, 216 (1951).