ether. Crystallization from acetone–ether mixtures gave 2.1 g. of colorless, fluffy needles in 90% yield, m.p. 230°.

Anal. Calcd. for $C_{29}H_{31}NO_2 \cdot HCl$: C, 69.9; H, 6.6; N, 2.8. Found: C, 69.9; H, 7.0; N, 3.0.

Acknowledgment.—We wish to acknowledge with thanks the suggestions, interest, and encouragement from Dr. Richard Baltzly in this work.

Condensations of Aromatic Aldehydes with Oxazolines and a New Synthesis of Cinnamic Acids

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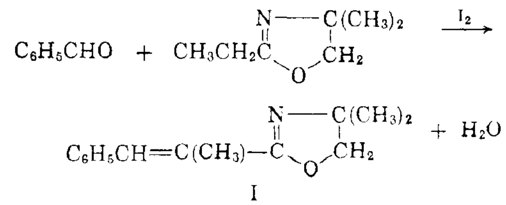
Benzaldehyde and other aromatic aldehydes have been condensed with a variety of 2-alkyl-2-oxazolines using suitable catalysts. Condensation occurs at the *alpha* position of the 2-alkyl substituent yielding phenylethenyloxazolines. Hydrolysis of these phenylethenyloxazolines gives the cinnamic acids in high yield.

According to a patent by Hamer and Rathbone[1] 2-methyl-2-oxazoline methiodide can be condensed with *p*-dimethylaminobenzaldehyde to yield the quaternary salt of 2-(2-*p*-dimethylaminophenylethenyl)-2-oxazoline.

Wiley and Bennett,[2] in referring to this work of Hamer and Rathbone, state that "condensations of this type have not been studied by other investigators or with compounds other than the alkiodides of 2-methyl-2-oxazoline". Cornforth[3] indicates that the work of Hamer and Rathbone "is a reaction which has no analogy among acyclic imino ethers."

2 - (1,1 - Dichloro - 2 - *p* - nitrophenyl - 2 - hydroxyethyl)-2-oxazoline has been prepared by the reaction of *p*-nitrobenzaldehyde with 2-dichloromethyl-2-oxazoline.[4] The reaction of an aromatic aldehyde with a nonquaternized alkyloxazoline to yield a phenylethenyloxazoline seemingly has not previously been reported.

Benzaldehyde was condensed with 2-ethyl-4,4-dimethyl-2-oxazoline. After twenty-three hours of reflux at temperatures of 133–153°, only a 16% yield of the desired 2-(1-methyl-2-phenylethenyl)-2-oxazoline (I) was isolated. Only a 32% yield of crude I was obtained when the reaction was carried out in the presence of acetic anhydride. A satisfactory reaction with a yield as high as 76% was achieved by the use of catalytic amounts of iodine (equation 1). Analytical results agree with the theoretical values. α-Methylcinnamic acid is obtained on acid-catalyzed hydrolysis (equation 2). Other catalysts for this reaction include *p*-xylenesulfonic acid, zinc chloride, and sodium bisulfate. These may be better than iodine but have not been studied as extensively. Sodium acetate was not an effective catalyst.



(1)

This condensation was successfully extended to other aldehydes and oxazolines. Hydrolysis of the phenylethenyloxazolines yielded the cinnamic acids without difficulty. The cinnamic acids obtained have melting points which agree with the literature values for products established as having, or provisionally assigned, the *trans* (phenyl/COOH) structure. Presumably the phenylethenyloxazolines have a *trans* (phenyl/oxazolyl) structure.

If the cinnamic acid is the desired product, it is convenient to hydrolyze the product mixture without isolation of the intermediate oxazoline derivative. This procedure is illustrated with *m*-nitrobenzaldehyde. At a 1:1 mole ratio of aldehyde to oxazoline, a 61% yield of α-methyl-*m*-nitrocinnamic acid was obtained. A 90% yield was obtained using a 1:2 mole ratio.

All of the other reactions were carried out at a 1:1 mole ratio. Further study of mole ratios, reaction conditions and catalysts would probably result in improved yields. The use of sodium bisulfate in place of iodine, for example, merits further attention.

This synthesis of cinnamic acids may be compared with that of Perkin[5] and Doebner.[6]

Experimental[7]

Starting Materials.—2-Ethyl-4,4-dimethyl-2-oxazoline and 2-ethyl-4-methyl-4-hydroxymethyl-2-oxazoline were

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[1] F. M. Hamer and R. J. Rathbone, British Patent 541,330 (1941).

[2] R. H. Wiley and L. L. Bennett, Jr., *Chem. Rev.*, **44**, 461 (1949).

[3] J. W. Cornforth, "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, ed., J. Wiley & Sons, Inc., New York, N. Y., 1957, p. 389.

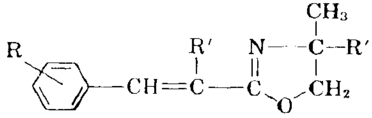
[4] H. Bretschneider, G. Piekarski, and K. Biemann, *Monatsh.*, **85**, 882 (1954); *Chem. Abstr.*, **49**, 15860 (1955).

[5] *Cf.* J. R. Johnson, "Organic Reactions," Vol. 1, Roger Adams, ed., J. Wiley & Sons, Inc., New York, N. Y., 1942, pp. 210–265.

[6] *Cf.* W. J. Gensler and E. Berman, *J. Am. Chem. Soc.*, **80**, 4949 (1958).

[7] All melting points were taken on a Fisher–Johns melting point apparatus.

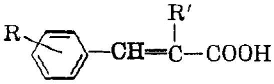
TABLE I



				Reaction					Calcd.		Found	
R	R′	R″	Catalyst	Time, hr.	Temp., °C.	Yield, %	B.p., °C. (mm.)	Formula	N	Neut. equiv.	N	Neut. equiv
H	CH_3	CH_3	None	23	133–153	16	109–110(0.3)	$C_{14}H_{17}NO$	...	215.3	...	230.5
H	CH_3	CH_3	Ac_2O(1 mole)	8	144–173	32 crude	107–125(2.0)	$C_{14}H_{17}NO$	...	215.3	...	269
H	CH_3	CH_3	NaOAc	23	132–152	15	102–111(0.3)	$C_{14}H_{17}NO$	...	215.3	...	236.3
H	CH_3	CH_3	I_2	23	136–156	68 (76 crude)	110–129(0.4)	$C_{14}H_{17}NO$	...	215.3	...	221.6
H	CH_3	CH_3	I_2	14	141–175	61 (70 crude)	111–118(1.0)	$C_{14}H_{17}NO$	6.51	215.3	6.72	217.4
H	CH_3	CH_3	$CH_3C_6H_4SO_3H$	15.5	143–157	82	114(0.6)–123(1.0)	$C_{14}H_{17}NO$	...	215.3	...	219.1
H	CH_3	CH_3	$ZnCl_2$	15.5	140–159	89	115(0.8)–118(1.0)	$C_{14}H_{17}NO$	...	215.3	...	217.8
H	CH_3	CH_3	$NaHSO_4$	15	143–164	90	117(0.9)–120(0.6)	$C_{14}H_{17}NO$	...	215.3	...	219.5
p-Cl	CH_3	CH_3	I_2	9	113–168	75 (84 crude)	133(1.0)–151(1.5)	$C_{14}H_{16}NOCl$	5.61	249.7	5.49	251.6
o-Cl	CH_3	CH_3	I_2	21.5	138–161	74	112(1.0)–133(0.5)	$C_{14}H_{16}NOCl$	5.61	249.7	5.86	264
											5.50	261
p-$(CH_3)_2N$	CH_3	CH_3	I_2	24	135–175	55	155(0.6)–163(0.3)	$C_{16}H_{22}N_2O$	10.84	129.2	11.47	136.3
m-NO_2	CH_3	CH_3	I_2	22	137–168	32[a]	155(0.6)–159(0.4)	$C_{14}H_{16}N_2O_3$	10.76	260.3, 265.7	10.80	261.3, 272
p-Cl	CH_3	CH_2OH	I_2	15.5	146–155	84	168(0.3)–182(0.6)	$C_{14}H_{16}NO_2Cl$[b]	...		...	
H	H	CH_3	I_2	8	125–146	77	112(0.4)–120(0.6)	$C_{13}H_{15}NO$	6.96	201.3	6.88	206.1
p-Cl	H	CH_3	I_2	9	117–149	70	140–160(0.9)	$C_{13}H_{14}NOCl$[c]	5.94	235.7	6.09	238.8

[a] Decomposition set in during initial distillation at pot temperature of *ca.* 220°. Crude distillate was redistilled to yield results reported. Better yields could be expected on repetition of this experiment. Calcd.: C, 64.60; H, 6.20. Found: C, 64.30; H, 6.44. [b] Calcd.: Cl, 13.34. Found: 12.38, 12.70. [c] Calcd.: Cl, 15.04. Found: 14.61.

TABLE II



R	R′	Yield, % a	Yield, % b	M.p., °C. Found[c]	M.p., °C. Lit. (ref.)	Neut. equiv. Calcd.	Neut. equiv. Found[c]
H	CH_3	92	83	80.5–81	80–81[d]	162.2	167.0
p-Cl	CH_3	92	69	166–167	166–167[d]	196.6	196.2
o-Cl	CH_3	99	73	108–109	109.5–110.5[d]	196.6	198.0
p-$(CH_3)_2N$	CH_3	80	44	210–211	204–204.5[d]	205.3	205.6[e]
m-NO_2	CH_3	94	30[f]	203–205	202–203[d]	207.2	208.4
H	H	97	75	134–135	133[g]	148.2	149.4
p-Cl	H	100	70	248–249	249–250[h]	182.6	182.9

[a] Based on oxazoline. Before recrystallization of the cinnamic acid. [b] Based on aldehyde. Before recrystallization of the cinnamic acid. [c] For recrystallized sample. [d] *Cf.* ref. 6. [e] Neut. equiv. as a base, 205.8. [f] *Cf.* footnote *a* of Table I. [g] "Dictionary of Organic Compounds," Vol. I, I. M. Heilbron and H. M. Bunbury, ed., Oxford University Press, New York, N. Y., 1953, p. 586. [h] J. K. Kochi, *J. Am. Chem. Soc.*, **78**, 1228 (1956).

prepared as previously described.[8] 2,4,4-Trimethyl-2-oxazoline[9] was prepared analogously by the reaction of acetic anhydride with 2-amino-2-methyl-1-propanol. A distilled product, b.p. 112–113°, of 99.2% purity was obtained in a 72% yield.

The aldehydes and other reagents were commercially available and were used without further purification.

Aldehyde–Oxazoline Condensation Reactions.—All of the iodine-catalyzed condensations were carried out according to the following general procedure. The aldehyde (1 mole), oxazoline (1 mole), and toluene (100 ml.) or in some instances benzene, were charged to a 500-ml. flask equipped with a sealed stirrer, thermometer, Vigreux column (18 in.), water separator (20 ml.), and reflux condenser. The mixtures were heated under reflux for several hours with azeotropic removal of water. If after several hours it was evident that water evolution was not proceeding at an appreciable rate, there was added 1 g. of iodine. Water evolution would start almost immediately.

The rate of water evolution usually became slower as the reaction progressed. Some attempts were made to speed up the reaction by increasing the reaction temperature (brought about by removal by distillation of part of the toluene) and by further additions of iodine. These methods were only moderately effective. Long reaction times still were required. Refluxing was continued until water elimination was essentially complete.

Reactions using catalysts other than iodine were conducted similarly except that the materials were added from the start of the run rather than after several hours of heating. Five grams each of xylenesulfonic acid, zinc chloride, and sodium bisulfate were used. Ten grams of sodium acetate was used.

After the water of reaction was removed, the mixtures were distilled at reduced pressure through an 18-in. Vigreux column. Some of the products could be solidified, but limited attempts to develop good methods of recrystallization were not very successful. All but the *p*-dimethylamino product would remain liquid for long periods unless special attempts at crystallization (seeding, cooling, etc.) were made. The *p*-dimethylamino derivative solidified to a low melting, yellow solid. Results are given in Table I.

Hydrolysis of Phenylethenyloxazolines to Cinnamic Acids.—The phenylethenyl-4,4-dimethyl-2-oxazolines were hydrolyzed to the cinnamic acids by the following procedure, used with but minor modifications for every example given.

The phenylethenyl-4,4-dimethyl-2-oxazoline (0.1 mole) was dissolved in 200 ml. of dilute hydrochloric acid (1 part concentrated hydrochloric acid to 3 parts water) and heated at reflux for 3 hr. The precipitated solid was collected by filtration, washed with two 50-ml. portions of water, and dried. This product (used as a basis for the reported yields) was recrystallized, generally from ethanol, to give a material with a melting point usually in close agreement with the melting point reported in the literature. Recrystallization was repeated until no change in melting point occurred. These products were then analyzed.

In the case of the *p*-dimethylamino derivative the pH of the mixture after hydrolysis was adjusted to 4 by the addition of aqueous sodium hydroxide solution. The precipitated solid was then collected, washed, dried and recrystallized as in the other examples. The results are given in Table II.

α-Methyl-*m*-nitrocinnamic Acid. Preparation without Isolation of Intermediate. I.—A mixture of 30.2 g. of *m*-nitrobenzaldehyde with 26 g. of 2-ethyl-4,4-dimethyl-2-oxazoline and 1 g. of sodium bisulfate in 100 ml. of toluene was heated under reflux with azeotropic removal of water as in the standard procedure. There was obtained 3.0 ml. of water in 5 hr. at pot temperatures of 118–179°. The mixture was cooled to 100° and a solution of 17 ml. of concd. sulfuric acid in 133 ml. of water was added in 5 min. The mixture was distilled until the remaining toluene was removed. The clear solution was refluxed for 1 hr. and left at room temperature overnight. An additional 100 ml. of water was added to the liquid–solid mixture, and refluxing was continued for 2 hr. The mixture was cooled to room temperature, the solid (A) was collected by filtration, washed with two 50-ml. portions of water and dried, finally in a vacuum oven at 55–60°. This material weighed 19.4 g. and had a melting point of 205–206°.

A second crop of product (B) (6.0 g., m.p. 204.5–205°) was obtained by refluxing the filtrate from A for 3 hr., cooling, filtering, washing, and drying as before. Recrystallization of A from 350 ml. of ethanol yielded 16.4 g. of product, m.p. 204–205°; neut. equiv. 207.0. The total of 25.4 g. corresponds to a 61% yield.

II.—A mixture of 60.4 g. of *m*-nitrobenzaldehyde with 104 g. of 2-ethyl-4,4-dimethyl-2-oxazoline and 3 g. of sodium bisulfate in 100 ml. of toluene was heated at reflux (130–137°) for 7 hr. with azeotropic removal of 7 ml. of water. Toluene and excess oxazoline were removed by distillation to a pot temperature of 182°. Water (100 ml.) was added and the remaining toluene (13 ml.) was removed by azeotropic distillation, with the water being returned to the pot. Concentrated hydrochloric acid (100 ml.) was added, and the mixture was heated at reflux for 6 hr., cooled, and filtered. The filter cake was washed with three 100-ml. portions of water and dried, finally in a vacuum oven at 55–60°.

This product weighed 74.4 g. (90% yield) and had a melting point of 196.5–198°. Recrystallization from ethanol yielded material with a melting point of 202–203° and a neutralization equivalent of 208.0.

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[8] H. L. Wehrmeister, *J. Org. Chem.*, **26**, 3821 (1961).

[9] P. F. Tryon, U.S. Patent 2,372,409 (1945).