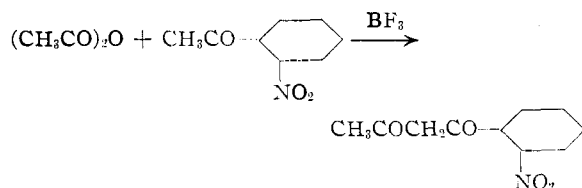


factory; this has been verified. Yields of 64–68% of the *o*-, *m*- and *p*-nitrobenzoylacetones have been obtained from the corresponding nitroacetophenones. The acetylation of *o*-nitroacetophenone may be represented as



Since the nitroacetophenones are readily prepared,⁵ the present method for preparing the nitro β -diketones is considered quite convenient.⁶

Gabriel and Gerhard⁷ have reported that *o*-nitrobenzoylacetone is reduced and cyclized in the presence of phosphorus and hydrogen iodide, or stannous chloride and acetic acid, to form 2-methyl-4-hydroxy-quinoline oxide. McCluskey⁸ found that this nitrogen oxide is converted to 2-methyl-4-hydroxy-quinoline on boiling with zinc dust and hydrochloric acid. We have found that the nitrogen oxide is similarly obtained from *o*-nitrobenzoylacetone using low pressure hydrogenation at 60° in the presence of Raney nickel or at room temperature using palladium charcoal (experiment by M. S. Bloom).

Experimental⁹

m-Nitroacetophenone (0.1 mole) was dissolved in 70 ml. (about 0.7 mole) of acetic anhydride, and the stirred mixture was saturated at 0° with boron trifluoride as described previously for similar acylations.^{4b} Then 700 ml. of 13% sodium acetate solution was added and the resulting mixture refluxed for twenty minutes. The mixture was chilled in an ice-bath and filtered. The precipitate was washed thoroughly with water, crushed in a mortar and dissolved in 300 ml. of cold 2% sodium hydroxide solution. The alkaline solution was shaken with ether. The ether phase was extracted with additional 2% alkali until it no longer gave a positive enol test. After filtering, the combined alkaline solution was chilled in an ice-bath and acidified with 10% sulfuric acid. The solid *m*-nitrobenzoylacetone was filtered off and recrystallized from 95% ethanol; yield, 64% melting at 113.5–114.5°; m. p. of copper salt, 277–278°.

In a similar manner, we prepared *p*-nitrobenzoylacetone in 66% yield, melting at 111.4–112.6° and after a second recrystallization at 112.0–112.8° (the copper salt darkened but failed to melt at 320°); also, we prepared *o*-nitrobenzoylacetone in 68% yield melting at 54–55° (catalytic reduction gave 2-methyl-4-hydroxyquinoline oxide, melting at 245–246°).⁹

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(5) See Walker and Hauser, *THIS JOURNAL*, **68**, 1387 (1946).

(6) *m*-Nitrobenzoylacetone has been prepared in 47% yield by the nitration of benzoylacetone (see reference 2). *o*-Nitrobenzoylacetone has been prepared by the acylation of acetoacetic ester with *o*-nitrobenzoyl chloride followed by abidic cleavage [Gevekoht, *Ann.*, **221**, 323 (1883), and Kermack and Smith, *J. Chem. Soc.*, 814 (1929)].

(7) Gabriel and Gerhard, *Ber.*, **54**, 1067 and 1615 (1921).

(8) McCluskey, *THIS JOURNAL*, **44**, 1577 (1922).

(9) Melting points are uncorrected.

The Inhalation Toxicity of Ketene and of Ketene Dimer

BY H. A. WOOSTER,¹ C. C. LUSHBAUGH AND C. E. REDEMAN²

The literature concerning the use of ketene in organic syntheses stresses its irritant qualities,^{3,4} but contains no detailed statement of its toxicity. Preliminary tests indicated that freshly generated ketene was highly toxic.⁵

Extended toxicity testing on mice, rats, guinea pigs and rabbits showed that ten minute exposures to concentrations of freshly generated ketene as low as 0.2 mg./liter (116 p. p. m.) may produce a high percentage of deaths in small animals. Diketene is less than 0.1 as toxic. These findings put ketene in the same order of toxicity as phosgene⁴ (0.2–2.0 mg./liter) and hydrogen cyanide⁶ (0.2–0.5 mg./liter). Death is from pulmonary edema and is entirely similar to, but much more rapid than is the case with phosgene poisoning. A complete report of this study will be made elsewhere.

(1) Present address: 706 Maloney Bldg., Hospital of the University of Pennsylvania, Philadelphia 4, Pa.

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(3) N. T. M. Wilmore, *J. Chem. Soc.*, **91**, 1938 (1907).

(4) C. D. Hurd and O. Kamm, "Organic Syntheses," Vol. IV, John Wiley and Sons, Inc., 1925, pp. 39–42.

(5) R. W. Gerard and W. Potts, personal communication.

(6) M. B. Jacobs, "Analytical Chemistry of Industrial Poisons, etc.," Interscience Publishers, Inc., 1941, p. 622.

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Direct Replacement of the Mesyloxy¹ Group by Cyanide

BY MORRIS ZIEF, HEWITT G. FLETCHER, JR., AND HOWARD R. KIRSHEIN

In the course of the preparation of several organic cyanides, our first approach to the synthesis of tetrahydrofurylacetonitrile by the replacement of the tosyloxy¹ group, followed the method described by Sekera and Marvel^{1a} for the preparation of *n*-cetyl cyanide and *n*-butyl cyanide. After this procedure failed, the fusion method suggested by the familiar reaction for the preparation of aryl cyanides by the fusion of the salts of aromatic sulfonic acids with potassium cyanide² proved successful. Fusion of tetrahydrofurfuryl tosylate with potassium cyanide produced a nine per cent. yield of the nitrile. When the mesyloxy¹ group, which in most instances has been shown to be more labile than the tosyloxy group,³ was substituted for the tosyloxy group, a 36% yield was obtained. When 6-tosyldiacetonegalactose, *n*-butyl tosylate or mesylate was fused with potassium cyanide, no reaction was observed. *s*-Butyl mesylate yielded considerable butene-2.

(1) "Tosyl" and "mesyl" are generally accepted abbreviations for *p*-toluenesulfonyl and methanesulfonyl, respectively.

(1a) Sekera and Marvel, *THIS JOURNAL*, **55**, 348 (1933).

(2) Merz and Mulhauser, *Ber.*, **3**, 710 (1870).

(3) Helferich and Gnuchtel, *ibid.*, **71**, 712 (1938).

Experimental

Tetrahydrofurfuryl Mesylate.—To a cooled solution of 51 g. (0.5 mole) of tetrahydrofurfuryl alcohol in 50 cc. of pyridine was added dropwise, with shaking, a mixture of 63 g. (0.55 mole) of mesyl chloride and 20 cc. of pyridine. After the reaction mixture had been allowed to stand in a refrigerator overnight, chopped ice and sufficient water to dissolve the pyridine hydrochloride were added. The product was extracted with four 40-cc. portions of chloroform. The chloroform extracts were combined and dried over anhydrous sodium sulfate. After removal of the chloroform, 64.2 g. (71%) of a product was obtained which boiled at 102–105° (2 mm.); n_D^{20} 1.4625.

Anal. Calcd. for $C_6H_{12}O_4S$: C, 40; H, 6.73; S, 17.8. Found: C, 39.7, 40.0; H, 6.96, 7.17; S, 17.7, 18.0.

Tetrahydrofurylacetonitrile.—Nine grams (0.05 mole) of the mesyl ester and 6.5 g. (0.1 mole) of potassium cyanide were placed in a 50-cc. round-bottomed flask and allowed to react on a steam-bath for four days. The contents of the flask were extracted with three 15-cc. portions of ether. The ether extracts were combined, dried and concentrated. Two grams of a colorless product, boiling at 45° (2 mm.), was collected; n_D^{15} 1.4490, 36% yield.⁴

s-Butyl Mesylate and Potassium Cyanide.—s-Butyl mesylate (15 g.) and potassium cyanide (10 g.) were heated at 100° in a flask connected to a gas washing bottle containing 8 cc. of liquid bromine in 200 cc. of carbon tetrachloride. After twenty-four hours the excess bromine was removed by treatment with sodium bisulfite. The mixture was washed with three 25-cc. portions of water, the carbon tetrachloride layer was dried over anhydrous sodium sulfate and concentrated at reduced pressure. A colorless liquid (8.1 g.), boiling at 160–161°, was obtained; yield of 2,3-dibromobutane was 38%.

Anal. Calcd. for $C_4H_8Br_2$: Br, 74.0. Found: Br, 73.8, 73.9.

(4) Barger, Robinson and Smith, *J. Chem. Soc.*, 718 (1937).

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Mannich Bases from Kojic Acid and Aryl Amines

By L. L. WOODS

Experiments have shown that kojic acid reacts with aryl amines and formalin to produce Man-

in considering the view that the hydroxyl at position 5 on kojic acid is phenolic^{1,2} and the recent results obtained by Holdren³ with furans it is not surprising that kojic acid possesses two centers of activity, positions 3 and 6; also, the only places where the reaction could take place without rearrangement. The compounds reported have been named on the assumption that such a structure is correct.

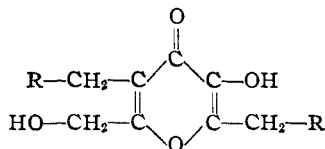
All of the Mannich bases produced by these experiments were crystalline. Three of the bases were light tan in color and soluble in acetone and ether. The aniline derivative which was greenish-yellow exhibited a sparing solubility in these solvents. When the bases were dissolved in dilute hydrochloric acid and a little ferric chloride added, a faint but unmistakable red coloration was obtained.

Procedures

Method A.—To 0.03 mole (4.23 g.) of kojic acid in 50 ml. of methanol about 3 ml. of concentrated hydrochloric acid was added, followed by 1 g. of paraformaldehyde and 0.03 mole of the aryl amine. The solution was then tested with congo red paper and if the solution was not acid sufficient hydrochloric acid was added to give an acid reaction. The resulting mixture was heated under reflux over a boiling water-bath for half an hour, cooled, and then poured into 300 ml. of water. The mixture was next made basic with ammonium hydroxide and allowed to stand overnight. Since the precipitated base adhered strongly to glass the supernatant liquid was decanted carefully. Purification of the material was effected by dissolving the base in warm dilute hydrochloric acid and then adding 300 ml. of water. The solution was filtered, made just basic with ammonium hydroxide and allowed to stand until precipitation appeared to be complete. The base was then obtained by filtration. In instances where the product was not crystalline and light tan in color, as in the case of the *p*-bromoaniline and methylaniline derivatives, the material was dissolved in the smallest amount of acetone possible and then precipitated with 300–400 ml. of water. Since this treatment caused the compounds to separate as a very finely divided precipitate it usually required several days standing before filtration. The bases were dried in the vacuum desiccator.

Method B.—To a mixture of 0.03 mole (4.23 g.) of kojic acid, 25 ml. of 37% formalin and about 3 ml. of concentrated hydrochloric acid, 0.03 mole of aryl amine was

TABLE I



R	Method	Yield, g.	M. p., ° C.	Formula	% Nitrogen ^c	
					Calcd.	Found
Anilino	A	5.2	263.9 charring	$C_{20}H_{20}N_2O_4$	7.95	7.87
Methylanilino	B	7.0	116–117 dec.	$C_{22}H_{24}N_2O_4$	7.38	7.33
<i>p</i> -Toluino	B ^a	5.1	148.4–148.9 dec.	$C_{22}H_{24}N_2O_4$	7.38	7.66
<i>p</i> -Bromoanilino	B	8.3	185.2 dec.	$C_{20}H_{18}N_2O_4Br_2$	5.49	5.43

^a Also by method A with poor yields. ^b Corrected, and melted with decomposition. ^c All nitrogen analyses were by the Kjeldahl method.

nich bases. Analysis of the resulting bases indicates that the reaction takes place not only at position 3, as expected, but at some other position also.

- (1) Tokuro Soda, *et al.*, *J. Chem. Soc. Japan*, **61**, 1227–1232 (1940),
(2) R. Adams, "Organic Reactions," Vol. 1, John Wiley and Sons, New York, N. Y., 1942, p. 311.
(3) Holdren and Hixon, *This Journal*, **63**, 1138, 1946.