

diketal (VIII, 1.62 g.) in dry tetrahydrofuran (40 ml.) was added boron trifluoride etherate (0.89 g.) in dry tetrahydrofuran (8.0 ml.) over 1 hr. under nitrogen. The reaction mixture was stirred for 2 more hours. Excess hydride was destroyed with acetone (2 ml.) and the mixture filtered. To the filtrate was added 1% ethanolic sodium hydroxide (10 ml.) and 30% hydrogen peroxide (0.7 g.), and the mixture heated on steam bath for 0.5 hr., cooled, diluted with water, and extracted with ether. The ether extracts were washed, dried, and the solvent removed to yield a colorless sirup. This was taken up in dry pyridine (10 ml.) and added to a freshly prepared complex of chromium trioxide (1.5 g.) and pyridine (15 ml.). The mixture was stirred overnight, filtered, and the residue washed with ether. The filtrate was diluted with water and extracted with ether. The ether extract was washed, dried, and the solvent removed. The residue was taken up in methanol (15 ml.) containing sodium (0.1 g.) and heated for 15 min. Concentration of the solution and subsequent cooling gave 0.52 g. of ketone (IX), m.p. 163–166°, and a second crop 0.09 g., m.p. 150–158°. Recrystallization gave an analytical sample m.p. 173–175°, $[\alpha]_D -11.8^\circ$, ν 1705 (C_6 -ketone) cm^{-1} .

Anal. Calcd. for $C_{25}H_{37}O_5$: C, 71.74; H, 9.15. Found: C, 71.57; H, 9.06.

Reaction of Some Indole Ketones with Iodine and Pyridine

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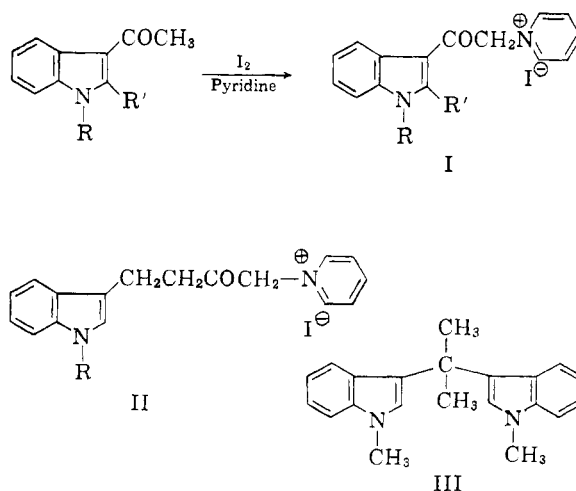
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The reaction of iodine and tertiary organic bases with an arylmethyl ketone² forming an *N*-(2-aryl-2-oxoethyl) quaternary salt of the base has been applied to heterocyclic ketones such as the 2-, 3-, and 4-pyridylmethyl ketones,^{3a} 2-thienylmethyl ketone,^{3b} and to several heterocyclic compounds where reaction occurs with a methyl group activated by being in the α - or γ -position to the heteroatom.²⁻⁴ This reaction offers a convenient method of converting such a methyl group into an aldehyde group.⁴

One of us recently⁵ utilized the reaction of 3-acetylindole with isoquinoline in a synthesis of hexadehydroyohimbane, and in this communication we wish to report some observations on the condensation of some other ketones of the indole series with pyridine and the usefulness of this reaction as a means of obtaining the corresponding carboxylic acids by the alkaline hydrolysis of these

salts.⁶ This latter reaction verifies the structures assigned to the quaternary salts. Those acids that are unsubstituted in the 2-position are especially readily available by this method. 3-Acetylindole, 1-methyl-3-acetylindole, and 2-methyl-3-acetylindole all reacted readily with iodine and pyridine forming the corresponding 1-(2-3'-indolyl-2-oxoethyl)pyridinium salts (I) in excellent yield. These salts were previously only available in poor yield by reaction of an indolymagnesium iodide with a haloacetyl halide and treatment of the resulting ω -halogeno ketone with pyridine.⁷ The exchange of the iodide anion for picrate or perchlorate anion was readily effected by treating an aqueous solution of the iodide with an aqueous solution of the appropriate acid. Ketones such as 4-indol-3-yl-2-butanone and 4-(1-methylindol-3-yl)-2-butanone which contain an aliphatic-type carbonyl group also underwent reaction but to a lesser degree. As acetone gives a dipyrindinium salt,^{3a} these ketones might be expected to react in a similar fashion. However, only a monopyridinium salt (II) was obtained and reaction occurred at the terminal methyl group as evidenced by the formation of the corresponding indole-3-propionic acids on alkaline hydrolysis. Variation of reaction solvent, temperature, or time failed to raise the yield of the pyridinium salt above 40%. Pyridinium hydroiodide (40% yield) was always isolated from this reaction; its identity was established by analytical and spectral data and by hydrolysis to pyridine. An equivalent quantity of unchanged ketone was usually recovered and accounted for the poor yield of the quaternary salt.



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(2) L. C. King, *J. Am. Chem. Soc.*, **66**, 894 (1944); L. C. King and M. McWhirter, *ibid.*, **68**, 717 (1946); J. L. Hartwell and S. R. L. Kornberg, *ibid.*, **68**, 868, 1131 (1946).

(3) (a) F. Kröhnke and K. F. Gross, *Chem. Ber.*, **92**, 22 (1959); (b) L. C. King, M. McWhirter, and R. L. Rowland, *J. Am. Chem. Soc.*, **70**, 240 (1948).

(4) J. Berson and T. Cohen, *J. Am. Chem. Soc.*, **78**, 416 (1956); W. Reid and H. Bender, *Chem. Ber.*, **89**, 1893 (1956); W. Reid and R. M. Gross, *ibid.*, **90**, 2646 (1957).

(5) D. R. Liljegen and K. T. Potts, *Proc. Chem. Soc.*, 340 (1960).

The hydrolysis of the pyridinium salts was readily effected by gently heating on a water bath with dilute alkali solution. Several incidental methods used for the preparation of acids for comparison purposes are described in the Experimental.

(6) F. Kröhnke, *Ber.*, **66**, 604 (1933).

(7) G. Sanna, *Gazz. Chim. Ital.*, **59**, 838 (1929); Q. Mingoia, *ibid.*, **61**, 646 (1931).

Experimental⁸

Methyl vinyl ketone was prepared by modification of the method of Wohl and Prill,⁹ anhydrous zinc chloride being used in the dehydration step. Care must be taken to remove completely all excess acetone. The methyl vinyl ketone was fractionated under reduced pressure (1.05 g., 30% yield) and distilled as a colorless liquid, b.p. 33–34°/130 mm., n_{20}^D 1.4070 (lit.¹⁰ reports b.p. 33–34°/130 mm., n_{20}^D 1.4086).

1-(2-3'-Indolyl-2-oxoethyl)pyridinium Iodide (I. R = R₁ = H).—3-Acetylidole¹¹ (1.6 g., 0.01 mole) was dissolved in pyridine (10 ml.) and iodine (2.55 g., 0.01 mole) added. The resulting solution was heated on a boiling water bath for 15 min. The excess of pyridine was evaporated and the solid residue triturated with water until it was quite friable. (Pyridinium hydroiodide was isolated from this aqueous phase.) Crystallization from water (charcoal) yielded 2.5 g. (71%) of the iodide as long, golden needles, m.p. 259°.

Anal. Calcd. for C₁₅H₁₅N₂OI: C, 49.5; H, 3.6; N, 7.7. Found: C, 49.5; H, 3.8; N, 7.4.

The picrate, prepared by the addition of a saturated aqueous solution of picric acid to a solution of the iodide in hot water, separated from water as fine, yellow needles, m.p. 224°.

Anal. Calcd. for C₂₁H₁₅N₃O₈: C, 54.2; H, 3.2; N, 15.05. Found: C, 54.6; H, 3.6; N, 14.9.

Similarly, **1-(2-1'-methyl-3'-indolyl-2-oxoethyl)pyridinium iodide (I. R = CH₃; R₁ = H)**, from 1-methyl-3-acetylidole,¹² separated from ethanol (charcoal) as pale yellow needles (69%), m.p. 233–234° dec.

Anal. Calcd. for C₁₆H₁₅N₂OI: C, 50.8; H, 4.0; N, 7.4. Found: C, 50.6; H, 4.5; N, 7.3.

1-(2-2'-Methyl-3'-indolyl-2-oxoethyl)pyridinium iodide (I. R = H; R₁ = CH₃), from 2-methyl-3-acetylidole,¹³ separated from water as yellow needles (69%), m.p. 275° dec. (*in vacuo*).

Anal. Calcd. for C₁₆H₁₅N₂OI: C, 50.8; H, 4.0; N, 7.4. Found: C, 50.7; H, 4.2; N, 7.3.

The picrate separated from ethanol as fine, yellow needles m.p. 195°.

Anal. Calcd. for C₂₂H₁₇N₃O₈: C, 55.1; H, 3.6; N, 14.6. Found: C, 55.6; H, 3.9; N, 14.8.

The perchlorate, prepared from the iodide by the addition of 50% aq. perchloric acid, formed white needles from aqueous ethanol, m.p. 275° (dec.).

Anal. Calcd. for C₁₆H₁₅N₂O₅Cl: C, 54.8; H, 4.3; N, 8.0. Found: C, 55.2; H, 4.5; N, 7.99.

1-(4-3'-Indolyl-2-oxobutyl)pyridinium Iodide (II. R = H).—4-Indol-3-yl-2-butanone¹⁴ (3.7 g., 0.02 mole) was dissolved in pyridine (100 ml.), iodine (5.0 g., 0.02 mole) added, and the mixture was heated on the boiling water bath for 30 min. Working up the reaction mixture as above and crystallization of the product from ethanol (charcoal) followed by recrystallization from aqueous ethanol gave 3.2 g. (41%) of pure iodide as golden yellow plates, m.p. 208°.

Anal. Calcd. for C₁₇H₁₇N₂OI: C, 52.0; H, 4.4; N, 7.1. Found: C, 51.9; H, 4.6; N, 6.7.

The washings from the trituration of the solid reaction product were filtered and evaporated to dryness. Crystallization of the solid residue from ethanol gave pyridinium hydroiodide (1.6 g., 40%), m.p. 260° (*in vacuo*) (lit.,¹⁵ m.p. ca. 268°).

(8) Melting points were determined on a hot stage, and evaporations were carried out under reduced pressure unless otherwise stated. Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne, Australia.

(9) A. Wohl and A. Prill, *Ann. Chem.*, **440**, 143 (1924).

(10) S. Krapinwin, *Chem. Zentr.*, 1336 I, (1910).

(11) G. Hart, D. R. Liljegren, and K. T. Potts, *J. Chem. Soc.*, 4267 (1961).

(12) Y. A. Baskakov and M. N. Mel'nikov, *Sbornik. Statei Obshechi Khim. Akad. Nauk S.S.S.R.*, **1**, 712 (1953); *Chem. Abstr.*, **49**, 1006^d (1955).

(13) K. T. Potts, *J. Org. Chem.*, **26**, 4719 (1961).

(14) J. Szmuszkovicz, *J. Am. Chem. Soc.*, **79**, 2819 (1957).

Anal. Calcd. for C₉H₉NI: C, 29.0; H, 2.9; N, 6.8; I, 61.3. Found: C, 29.4; H, 3.1; N, 6.1; I, 61.6.

Ultraviolet spectrum: λ_{max} 252, 257, 290, 359 m μ ; ϵ 9630, 9900, 690, and 350.

Treatment with alkali gave pyridine which was identified by paper chromatography, using Whatman's No. 1 paper and butanol:water:hydrochloric acid (4:3:1) as solvent.¹⁶

The corresponding 1-methyl compound (II. R = CH₃) was similarly prepared from 4-(1-methylindol-3-yl)-2-butanone described below. Purification to analytical purity could not be achieved and it was hydrolyzed directly to the corresponding propionic acid.

4-(1-Methylindol-3-yl)-2-butanone. (a)—Following the method described by Szmuszkovicz,¹⁴ for the preparation of 4-indol-3-yl-2-butanone 1-methylindole¹⁷ (13.1 g., 0.1 mole) and methyl vinyl ketone (21.0 g., 0.3 mole) gave, after isolation of the product by ether extraction and work-up in the usual way, a dark red oil that distilled as a pale lemon, mobile oil, b.p. 138–140°/0.2 mm., 13.5 g. (67%). An analytical sample distilled at 120°/0.1 mm., n_{20}^D 1.5717.

Anal. Calcd. for C₁₃H₁₅NO: C, 77.6; H, 7.5; N, 6.96. Found: C, 77.4; H, 7.4; N, 7.0.

The semicarbazone separated from aqueous ethanol as white, irregular prisms, m.p. 197°.

Anal. Calcd. for C₁₄H₁₈N₄O: C, 65.1; H, 7.0; N, 21.7. Found: C, 65.05; H, 7.1; N, 21.9.

In an experiment in which the methyl vinyl ketone used was later found to be contaminated with acetone, the residue remaining in the distillation flask was dissolved in ethanol and the purple solution allowed to stand overnight. An orange solid separated which after several crystallizations from ethanol (charcoal) formed pale fawn needles, m.p. 150°. The NMR spectrum¹⁸ showed bands at τ 3.35 (α indole proton), τ 6.55 (N—CH₃ protons), τ 8.23 (C—CH₃ protons), and the relative intensities of the bands indicated the presence of two such groups. This product is regarded as 3,3'-isopropylidenebis(1-methylindol) (III) which has recently been reported¹⁹ to be formed from 1-methylindole and acetone in the presence of ethanolic hydrogen chloride or acetic acid (m.p. reported 151–152°).

Anal. Calcd. for C₂₂H₂₂N₂: C, 83.4; H, 7.3; N, 9.3. Found: C, 83.3; H, 7.1; N, 9.4.

(b) **Methylation of 4-Indol-3-yl-2-butanone.**—Small pieces of clean, dry sodium (4 g., 0.08 g.-atom) were dissolved in liquid ammonia (200 ml.) containing a crystal of ferric nitrate nonahydrate with vigorous stirring. The ketone (3.7 g., 0.02 mole) in dry ether (50 ml.) was added over a 10-min. period, followed by the dropwise addition of methyl iodide (12.5 g., 0.08 mole) in an equal volume of dry ether. After 30 min., stirring was discontinued and the ammonia allowed to evaporate. Water (100 ml.) followed by ether (100 ml.) was added to the residue, the aqueous phase extracted with more ether (3 \times 50 ml.) and the combined ether extracts were washed with water (2 \times 50 ml.). After drying over anhydrous sodium sulfate, the ether solution was evaporated, and the residual light brown oil distilled *in vacuo* as a very pale yellow oil, b.p. 120°/0.1 mm., in practically quantitative yield. This oil was always contaminated with a co-distilling, more fully methylated product in just sufficient quantity to give analytical results slightly high in carbon and hydrogen. The four-fold excess of sodamide and methyl iodide was essential to obtain a fully ind-N-methylated product and undoubtedly gave rise to some C-methylated product. However, repeated distillation *in vacuo*

(15) P. F. Trowbridge, *ibid.*, **19**, 327 (1897).

(16) W. H. F. Sasse, *J. Chem. Soc.*, 526 (1960).

(17) K. T. Potts and J. E. Saxton, *Org. Syn.*, **40**, 68 (1960).

(18) Measured in carbon disulfide at 60 Mc. with a Varian Model V-4302 spectrometer, using internal TMS as reference. We thank Dr. T. H. Crawford for measuring this spectrum.

(19) W. E. Noland, C. G. Richards, H. S. Desai, and M. R. Venkiteswaran, *J. Org. Chem.*, **26**, 4254 (1961); see also M. Scholtz, *Ber.*, **46**, 1088 (1913).

TABLE I
INDOLE ACIDS OBTAINED BY THE ALKALINE HYDROLYSIS OF SOME 3'-INDOLYL-2-OXOALKYL-PYRIDINIUM SALTS

Pyridinium salt used	Acid obtained	M.p.,* °C.	Yield, %	Formula	Calcd.			Found		
					C	H	N	C	H	N
2-3'-Indolyl-2-oxoethyl-	Indole-3-carboxylic acid	220 ^a	87	C ₉ H ₇ NO ₂	67.1	4.4	8.7	67.5	4.8	8.6
2-1'-Methyl-3'-indolyl-2-oxoethyl-	1-Methylindole-3-carboxylic acid	214 ^b	90	C ₁₀ H ₉ NO ₂	68.6	5.2	8.0	68.7	5.0	7.8
2-2'-Methyl-3'-indolyl-2-oxoethyl-	2-Methylindole-3-carboxylic acid	180 ^c	90	C ₁₀ H ₉ NO ₂	68.6	5.2	8.0	68.9	5.3	8.5
4-3'-Indolyl-2-oxobutyl-	Indole-3-propionic acid	134 ^d	93	C ₁₁ H ₁₁ NO ₂	69.8	5.9	7.4	69.4	5.9	7.3
4-1'-Methyl-3'-indolyl-2-oxobutyl	1-Methylindole-3-propionic acid	125 ^e	20 ^f	C ₁₂ H ₁₃ NO ₂	70.9	6.45	6.9	70.5	6.6	6.8

* *In vacuo*. ^a Lit.,²² m.p. 218°. ^b Lit.,²¹ m.p. 212° dec. ^c Lit.,²³ m.p. 176-177°. ^d Lit.,²⁴ m.p. 134°. ^e Lit.,²⁰ m.p. 125.5-126°. ^f Hydrolysis effected without purification of the pyridinium salt.

gave a pure product identical with that prepared by method (a).

Alkaline Hydrolysis of the Pyridinium Salts. General Procedure.—The pyridinium salt (0.01 mole) was dissolved in aqueous ethanol (60 ml. of 50%) and the solution was warmed gently with sodium hydroxide (3 g.) for 10 min. (30 min. with the propionic acids). After cooling and acidification with hydrochloric acid, the solution was extracted with ether (3 × 50 ml.) and the ether extract was dried (sodium sulfate) and evaporated to dryness. Crystallization of the solid residue from water or acetone-water (charcoal) usually afforded the acid as white crystals. Identification was established by analytical data, mixed m.p. determinations, and comparison of infrared spectra with those of authentic specimens.

1-Methylindole-3-propionic Acid.—1-Methylindole (2.6 g., 0.02 mole), acetic acid (12 ml.), acetic anhydride (4 ml.), and commercial acrylic acid (4.3 g., 0.06 mole) were heated on a boiling water bath for 3 hr. The volatile material was then removed and the thick, blue residue added to a solution of sodium hydroxide (2.5 g.) in water (20 ml.). After cooling, the solution was filtered and the filtrate acidified with 2 *N* hydrochloric acid. The precipitated acid was collected, washed well with water, and recrystallized from water (charcoal) whence it separated as long, white needles, 2.4 g., 60%, m.p. 125° (lit.,²⁰ m.p. 125.5-126°).

Anal. Calcd. for C₁₂H₁₃NO₂: C, 70.9; H, 6.45; N, 6.9. Found: C, 70.7; H, 6.3; N, 7.4.

1-Methylindole-3-carboxylic Acid.—A sample of this acid was prepared in good yield by oxidation of 1-methylindole-3-aldehyde with alkaline potassium permanganate at 60° and isolation of the product in the usual way for this type of reaction. Crystallization from acetone-water gave pale cream plates, m.p. 214° (*in vacuo*) (lit.,²¹ m.p. 212° dec.).

(20) H. R. Snyder and E. L. Eliel, *J. Am. Chem. Soc.*, **71**, 663 (1949).

(21) W. B. Whalley, *J. Chem. Soc.*, 1651 (1954).

(22) C. Zatti and A. Furante, *Ber.*, **23**, 2296 (1890).

(23) A. Angeli, *Gazz. chim. ital.*, **22** II, 20 (1892).

(24) A. Ellinger, *Ber.*, **38**, 2884 (1905).

Desulfurization of Thiiranes with Iodine

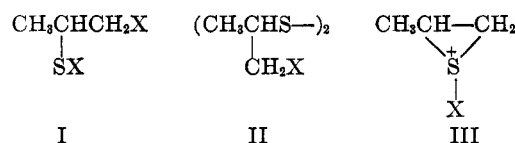
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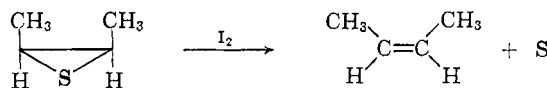
The reaction of chlorine and bromine with propylene sulfide has been shown to result in ring opening with the formation of a β-halosulphenyl

halide, I, or the corresponding disulfide, II, depending on the conditions employed.¹ An *S*-halo



intermediate, III, was postulated for the reactions. In a more recent investigation equilibrium constants were determined for the formation of iodine complexes of cyclic sulfides,² and it was observed that thiacyclobutane polymerized readily in carbon tetrachloride solutions of iodine. However, in neither instance was there any report of the iodine-thiirane system. The possibility of an interaction or reaction between iodine and 2,3-dimethylthiirane was of interest to us because the desulfurization of the latter with methyl iodide led under certain conditions to the formation of molecular iodine.³

We wish to report that iodine reacts with *meso*- and *DL*-2,3-dimethylthiirane in solvents such as refluxing acetone or benzene with stereospecific loss of sulfur to yield butene and elementary sulfur in moderate yield. Although some molecular iodine is consumed in the process, an iodine/sulfide molar ratio of less than 0.5 is sufficient to carry out the desulfurization.



Thiirane isomers were prepared from *cis*- and *trans*-2-butene by the thiourea method⁴ as reported previously.³ The initial alkenes contained less than 0.6% of the contaminating stereoisomer, and the composition of the butene products, determined on a silicone or dimethyl sulfolane chromatographic column, is given in Table I. No *C-4* isomers other than *cis*- and *trans*-2-butene were detected.

(1) J. M. Stewart and H. P. Cordts, *J. Am. Chem. Soc.*, **74**, 5880 (1952).

(2) J. D. McCullough and D. Mulvey, *ibid.*, **81**, 1291 (1959).

(3) G. K. Helmkamp and D. J. Pettitt, *J. Org. Chem.*, **25**, 1754 (1960).

(4) F. G. Bordwell and H. M. Andersen, *J. Am. Chem. Soc.*, **75**, 4959 (1953).