EXPERIMENTAL

The following procedure was used, in general, in preparing the derivatives given in Table I.

TABLE I

MELTING POINTS[a] AND LITERATURE VALUES

Compound	M.P.	Lit., °C.
methyl *n*-hexyl ketone[b]	58–59	58[k]
methyl isobutyl ketone[b]	92–93[h]	95[k]
methyl isopropyl ketone[b]	123–124	117[k], 119–120[m]
acetone[b]	125–126	126[k]
acetone[b,e]	124–126	126[k]
cyclohexanone[c]	160–161	161[k]
acetaldehyde[b]	165–166[i]	168[k]
formaldehyde[b]	165–166	166[k]
benzaldehyde[d]	238–240	237[k]
benzaldehyde[c,e]	239–240	237[k]
benzaldehyde[d,f]	239–240	237[k]
benzaldehyde[d,g]	239–240	237[k]
acetophenone[d]	247–248	250[k]
cinnamaldehyde[d]	255–256	255[k]
methyl *p*-tolyl ketone[d]	257–259[j]	260[k]
methyl *p*-tolyl ketone[c,e]	247–254	260[k]
7-ethyltetralone-1[d]	271–272	275[n]
7-ethyltetralone-1[c,e]	273–274	275[n]
p-hydroxybenzaldehyde[d]	284–284.5	280[k]

[a] Uncorrected. [b] Dilution with water needed to precipitate derivative. [c] Derivative crystallized out slowly. [d] Derivative precipitated immediately on adding acid. [e] Ten drops of acetic acid used instead of hydrochloric acid. [f] Triglyme solution of reagent. [g] Tetrahydrofuran solution of reagent. [h] Recrystallized from ethanol: m.p. before was 86–89°. [i] Recrystallized from ethanol; m.p. before was 153–154°. See ref. 4, p. 586. [j] Recrystallized from diglyme: m.p. before was 249–256°. [k] Ref. 1. [m] Ref. 4. [n] This was prepared in these laboratories by a conventional technique and recrystallized from ethyl acetate. Calcd. for $C_{18}H_{18}N_4O_4$: C, 61.01; H, 5.12; N, 15.80. Found[9]: C, 61.21; H, 5.19; N, 15.51.

A solution of 4 g. of 2,4-dinitrophenylhydrazine was prepared by warming in 120 ml. of diglyme and allowed to stand at room temperature for several days. Five ml. of this solution, at room temperature, was added to approximately 0.1 g. of the carbonyl compound dissolved in 1 ml. of 95% ethanol. Where the carbonyl compound was insoluble in 95% ethanol it was dissolved in diglyme, as, for example, in the case of *p*-hydroxybenzaldehyde. Three drops of concentrate hydrochloric acid were then added, causing the immediate formation of the derivative. In some cases the derivative precipitated immediately, in others dilution with water was necessary, while in one the derivative crystallized out slowly. The derivative was filtered, washed with ethanol or aqueous ethanol and dried by suction. In only three cases was it necessary to recrystallize the derivative to obtain a satisfactory melting point. Thus, the new technique gave *excellent crudes* in most cases, within a few minutes work.

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(9) Schwarzkopf Laboratories, Woodside 77, N. Y.

Oxidation of Methyl 8-Nitrodehydroabietate. II[1]

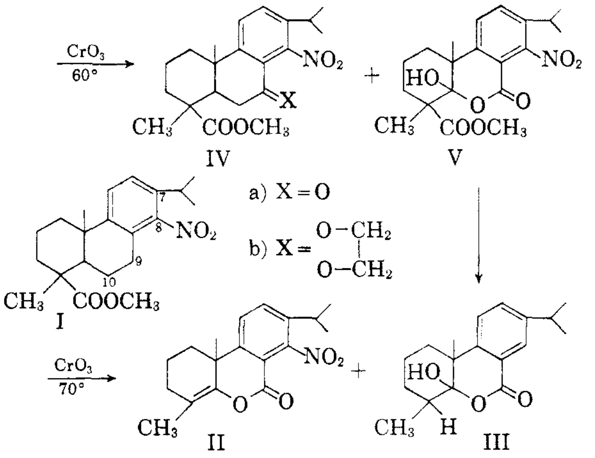
WILLIAM J. CONSIDINE[2] AND H. H. ZEISS

Received August 25, 1958

We wish to report the results of a study of the oxidation of methyl 8-nitrodehydroabietate I with chromium trioxide at 60°. The oxidation of I with this trioxide at 70° has been shown to involve the destruction of the hydrophenanthrene system, and the products of the oxidation have been formulated as the ketol lactone III and the enol lactone II arising from III by dehydration.[1] It has now been found possible to isolate compounds IVa and V from oxidations at 60° as intermediates in the formation of the ketol lactone III.

The neutral fraction of the oxidation mixture in the present work consists of methyl 9-oxo-8-nitrodehydroabietate IVa and is characterized by way of its 2,4-dinitrophenylhydrazone and ethylene ketal derivatives. The ultraviolet spectrum of IVa is consistent with this formulation, since the conjugation of the carbonyl function at C-9 with the phenyl ring causes a shift in the positions of the absorption maxima of methyl 8-nitrodehydroabietate I as well as a large increase in the intensity of absorption (see Table I). Formation of the ethylene ketal IVb blocks this conjugation and its spectrum is very similar to that of I, although a small bathochromic shift is noticed in this case owing to the presence of the polar ketal group. The infrared spectrum (Table I) of the ketone IVa also shows the presence of the conjugated ketonic system by an absorption band at 5.91μ.

FIGURE I



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(1) Paper I: H. H. Zeiss and M. Tsutsui, *J. Am. Chem. Soc.*, **77**, 6707 (1955).

(2) Felton Chemical Co., Inc., 599 Johnson Ave., Brooklyn 37, N. Y.

TABLE I

SPECTRAL DATA

Compound	Ultraviolet		Carbonyl stretch (μ)
	$\lambda_{max}^{95\% \text{ EtOH}}$	mμ (log ϵ)	
I	264(2.88)	272(2.81)	5.81
IVa	245(3.93)	300(3.33)	5.80, 5.91
IVb	269(2.77)	277(2.79)	5.80

The acidic fraction of the oxidation mixture consists of a monobasic acid, according to analytical data, containing one less carbon atom than the starting material I. The infrared spectrum of this compound V is remarkable in that the hydroxyl region shows resolution into two peaks at 2.94μ and 3.05μ. Since compounds of the ketol lactone type, *e.g.*, III, have similar spectra,[1,3] this acid is formulated as V. In order to further establish this structure, V was refluxed with acetic acid containing Cr^{3+} ion. Under these nonoxidizing conditions solvolysis of the methyl ester and decarboxylation occur with formation of the known compound III.

The isolation of IVa and V from I provides further insight into the processes which lead to the destruction of the diterpenic acid ring system during vigorous oxidation. The first point to be attacked is the benzyl carbon at C-9. Further oxidation of the 9-oxo compound thus formed gives rise to the ketol lactone V which in turn is shown to lead to the ketol lactone III on further heating in acetic acid.

EXPERIMENTAL[4]

Methyl 8-nitrodehydroabietate (I). Methyl 8-nitrodehydroabietate was made by the method of Campbell and Morgana.[5] The infrared spectrum showed absorptions at 5.81μ and 6.56μ. The ultraviolet spectrum showed: $\lambda_{max}^{95\% \text{ EtOH}}$ 264 mμ(log ϵ 2.88), 272 mμ(log ϵ 2.81).

Oxidation of methyl 8-nitrodehydroabietate. Methyl 8-nitrodehydroabietate (1.0 g., 2.8 mmole) was dissolved in 50 ml. of glacial acetic acid contained in a three-neck flask immersed in a bath held at 60°. During stirring a solution of chromic acid (1.12 g., 10.8 mmole) in the minimum amount of water necessary to achieve solution and 20 ml. of glacial acetic acid was added over the course of 2 hr. Stirring was continued for an additional 6 hr. The acetic acid was removed at aspirator pressure and the residue was taken up in ether and washed with water (discard) until the washings were colorless (removal of Cr^{3+}). The ether was then washed with a 1% sodium carbonate solution (to *p*H 10). This alkaline extract is discussed further under *Acidic fraction.*

(a) *Neutral fraction* [*Methyl 9-oxo-8-nitrodehydroabietate* (IVa)]. The ether solution was dried over anhydrous potassium carbonate and the solvent evaporated to give 0.63 g. (1.7 mmole) of a yellow solid, yield 63%. Recrystallization from methanol gave yellow plates, m.p. 195–196.5°, [α] +153.5° (C = 0.945).

Anal. Calcd. for $C_{21}H_{27}NO_5$: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.39; H, 7.38; N, 3.51.

The infrared spectrum showed absorption at 5.80μ, 5.91μ and 6.49μ. The ultraviolet spectrum showed: $\lambda_{max}^{95\% \text{ EtOH}}$ 245 mμ(log ϵ 3.93), 300 mμ(log ϵ 3.33).

The *2,4-dinitrophenylhydrazone* derivative was obtained as red needles, m.p. 193–194.5°, after recrystallization from methanol.

Anal. Calcd. for $C_{27}H_{31}N_5O_8$: C, 58.58; H, 5.64; N, 12.65. Found: C, 58.51; H, 5.41; N, 12.38.

(b) *Acidic fraction* [*Methyl 9-oxo-10-oxa-11-hydroxy-8-nitrodehydroabietate* (V)]. The alkaline extract from above was filtered and heated. While boiling, enough 1% hydrochloric acid was added to just cause turbidity. The resulting suspension was cooled, filtered by suction, and dried. A light brown solid was obtained, yield (0.195 g., 0.48 mmole) 18%.

Recrystallization from methanol gave light tan prisms, m.p. 183.25–184.5°, [α] −201° (C = 1.00).

Anal. Calcd. for $C_{20}H_{25}NO_7$: C, 61.37; H, 6.44; N, 3.58. Found: C, 61.44; H, 6.17; N, 3.85, 3.44.

Saponification equivalent, Calcd. 391. Found 379.

The infrared spectrum had absorption at 2.94μ, 3.05μ, 5.81μ, 5.89μ, and 6.50μ. The ultraviolet spectrum showed $\lambda_{max}^{95\% \text{ EtOH}}$ 294 mμ(log ϵ 3.79).

Methyl 9-ethylene ketal-8-nitrodehydroabietate (IVb). Methyl 9-oxo-8-nitrodehydroabietate (IVa) (0.95 g., 2.5 mmole) was refluxed for 24 hr. with a solution of *p*-toluenesulfonic acid monohydrate (200 mg.) in a mixture of 40 ml. of benzene and 20 ml. of ethylene glycol. The apparatus was arranged for the continuous removal of water from its azeotrope with benzene. The *p*-toluenesulfonic acid was neutralized with methanolic potassium hydroxide and the reaction mixture was poured into 100 ml. of benzene. The benzene was washed with six portions of water and dried over anhydrous potassium carbonate. Removal of the benzene at the water pump gave oily crystals. By recrystallization from methanol 0.37 g. (0.89 mmole, 36%) of white plates were obtained, m.p. 203.5–204.5°. Recrystallization from hexane gave white plates, m.p. 204.5–206°; [α] 142° (C = 0.55).

Anal. Calcd. for $C_{23}H_{31}NO_6$: C, 66.16; H, 7.48; N, 3.36. Found: C, 66.39; H, 7.28; N, 3.19.

The infrared spectrum showed absorption at 5.80μ, 6.54μ, and 9.24μ. The ultraviolet spectrum showed $\lambda_{max}^{95\% \text{ EtOH}}$ 269 mμ(log ϵ 2.77), 277 mμ(log ϵ 2.79).

Hydrolysis of methyl 9-ethylene ketal-8-nitrodehydroabietate. Methyl 9-ethylene ketal-8-nitrodehydroabietate (IVb) (24 mg., 0.06 mmole) was dissolved in a mixture of 5 ml. of glacial acetic acid and 1 ml. of water. The solution was heated on the steam bath for 0.5 hr. and while still hot, water was added dropwise until turbidity persisted. The reaction mixture was cooled, and filtered by suction. The filter cake was washed with water, dried, and recrystallized from methanol to give yellow plates, m.p. 191.5–193°. The yield (15 mg., 0.035 mmole) was 60%. The infrared spectrum of this material is identical with that of authentic methyl 9-oxo-8-nitrodehydroabietate (IVa).

Solvolysis of methyl 9-oxo-10-oxa-11-hydroxy-8-nitrodehydroabietate (V). Methyl 9-oxo-10-oxa-11-hydroxy-8-nitrodehydroabietate (V) (0.24 g., 0.61 mmole) was dissolved in 25 ml. of glacial acetic acid. Chromium oxide (0.24 g., 1.58 mmole) was added and the reaction mixture was refluxed for 17 hr.

The acetic acid was removed at aspirator pressure and the residue heated to 150° for 5 min. while still under vacuum. The solid was taken up in ether and the ether solution was washed with 5% aqueous sodium hydroxide until alkaline to litmus. The alkaline extract was boiled for 5 min., cooled, and then acidified with 5% hydrochloric acid.

The precipitate formed was filtered by suction and dried. A white powder was obtained, yield (0.11 g., 0.34 mmole)

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(3) E. S. Hansen and H. H. Zeiss, *J. Am. Chem. Soc.*, **77**, 1643 (1955).

(4) All melting points are corrected. All infrared spectra were taken in chloroform, ultraviolet spectra in 95% ethanol and rotations (D line) in chloroform. Microanalyses were performed by the Schwartzkopf Microanalytical Laboratories, Woodside 77, New York, N. Y.

(5) W. Campbell and M. Morgana, *J. Am. Chem. Soc.*, **63**, 1838 (1941).

52%. Recrystallization from 95% ethanol gave white prisms, m.p. 230–231° (lit.[3] 231–232°). The infrared spectrum showed absorption at 2.79μ, 2.99μ, 5.78μ, 6.42μ and was identical with that of an authentic sample of 1,12-dimethyl-7-isopropyl-9-oxo-10-oxa-11-hydroxy-8-nitro-1,2,3,4,9,10,-11,12-octahydrophenanthrene (III).[6] The ultraviolet spectrum showed: $\lambda_{max}^{95\%\ EtOH}$ 293 mμ(log ϵ 3.19).[6]

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(6) M. Tsutsui, Ph.D. Thesis, Yale University, 1955.

Photochemical Oxidation of 5-Nitro-2-furfuryl Iodide

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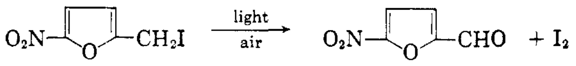
Received August 25, 1958

The oxidation of certain substituted bromomethanes to aldehydes by means of dimethyl sulfoxide was recently described by Kornblum and associates.[1] We wish to report a formally similar reaction, the photochemical air oxidation of 5-nitro-2-furfuryl iodide, I, to 5-nitro-2-furfural, II, and iodine.



I II

The synthesis of I was desirable in connection with this laboratory's continuing interest in chemotherapeutic nitrofurans.[2] It was readily effected by the reaction of 5-nitro-2-furfuryl nitrate with sodium iodide in acetone.

Chloroform solutions of I were stable for at least 2 weeks in the dark but liberated iodine when exposed to light. This was accompanied by the appearance of a new peak at 5.89μ in the infrared spectrum, corresponding to the carbonyl absorption of II. Treatment of the crude iodine-free product with semicarbazide hydrochloride gave the semicarbazone of II, although in unsatisfactory yield. As an estimate of the time necessary for completion of the reaction and a more quantitative estimate of the yield was desired, the reaction rate was followed by sodium thiosulfate titration and by infrared analysis of the reaction mixture. The results showed the reaction to be essentially complete in 70 hr., and the maximum yield of II to be 54%. By chromatography on alumina a 34% yield of II was isolated and identified by its infrared spectrum and conversion to 5-nitro-2-furfural phenylhydrazone in 90% yield.

EXPERIMENTAL[3,4]

5-Nitro-2-furfuryl nitrate. To 720 ml. of acetic anhydride was added, with stirring, 189 g. (2.1 moles) of concentrated nitric acid followed by 108 g. (1.1 mole) of furfuryl alcohol. The temperature was held at 20–25° by means of an ice bath. The total time of addition was 12–15 min. The mixture was heated to 40° for 1 hr. and then cooled to 25°. One l. of water and 300 g. of trisodium phosphate were added and the temperature was raised to 60° for 1 hr., cooled to 10–15° and the solid which separated was collected. The yield was 88 g. (42%) m.p. 34–36°. Recrystallization from isopropyl alcohol raised the m.p. to 36–36.5°.

Anal. Calcd. for $C_5H_4N_2O_6$: C, 31.92; H, 2.14; N, 14.89. Found: C, 32.05; H, 2.34; N, 14.75.

5-Nitro-2-furfuryl iodide. A solution of 179 g. (0.95 mole) of 5-nitro-2-furfuryl nitrate in 250 ml. of acetone was added to a saturated solution of 150 g. (1.00 mole) of sodium iodide in acetone. After standing in the cold for 6 hr. the sodium nitrate was removed by filtration and the acetone was evaporated from the filtrate at 30° by means of a rotary evaporator. The residue was diluted with 100 ml. of isopropyl alcohol and chilled. The orange crystals were collected, washed with a little isopropyl alcohol and dried. The yield was 184 g. (76%) m.p. 58–59°.

Anal. Calcd. for $C_5H_4INO_3$: C, 23.74; H, 1.59; N, 5.54; I, 50.17. Found: C, 23.91; H, 1.53; N, 5.64; I, 50.4.

Rate determinations. Two 1-l. 1% chloroform solutions of 5-nitro-2-furfuryl iodide were allowed to stand 70 hr. in 2-l. Erlenmeyer flasks continually exposed to laboratory light. Periodically 10-ml. aliquots were removed and titrated with 0.1*N* sodium thiosulfate to the disappearance of the pink color. Infrared spectra,[5] were determined in 0.5-mm. matched sodium chloride cells with chloroform in the solvent cell. A standard curve of analytically pure 5-nitro-2-furfural was prepared and was shown to obey Beer's Law over the concentration range studied.

Isolation and characterization of 5-nitro-2-furfural. After 90–100% of the iodine had been liberated, the two solutions were combined and shaken with 200 ml. of 10% sodium thiosulfate solution to remove the iodine. The chloroform layer was separated, dried, and the chloroform removed at 30–40° by a rotary vacuum evaporator. The residue was 10 g. of dark, golden liquid. Several small-scale experiments indicated that purification could be effected by chromatography and the remaining product, 7.21 g., in about 50 ml. of benzene was added to a column containing 500 g. of acid-washed alumina. Development and elution with benzene yielded 1.54 g. of slightly impure 5-nitro-2-furfuryl iodide, m.p. 49–52, in the 350 ml. of eluent. The next 2 l. of benzene yielded 2.46 g. of 5-nitro-2-furfural. The infrared spectrum of this sample was identical with the spectrum of authentic 5-nitro-2-furfural. The corrected yield, based on unrecovered 5-nitro-2-furfuryl iodide, was 34%. To provide a solid derivative, the product was dissolved in ethanol and treated with an aqueous solution containing 2.5 g. of phenylhydrazine hydrochloride. The red precipitate was collected, washed with ethanol and water, and dried at 60°. The yield was 3.5 g. (90%) m.p. 190–192°. λ_{max}^{EtOH} 465 mμ (log ϵ 4.32).

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(1) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957).

(2) For a recent paper in this series, see J. G. Michels and G. Gever, *J. Am. Chem. Soc.*, **78**, 5349 (1956).

(3) All melting points were taken on a calibrated Fisher-Johns apparatus.

(4) Microanalyses were carried out by Mr. Gordon Ginther and the ultraviolet spectra were determined by Mr. Curtis Eaton and Mrs. Catherine Gravesen.

(5) A Perkin-Elmer Model 21 instrument employing sodium chloride optics was used.