[CONTRIBUTION FROM THE NAVAL STORES STATION, U. S. DEPARTMENT OF AGRICULTURE[1]]

Air Oxidation of Resin Acids. I. Photo-sensitized Oxidation of Levopimaric Acid

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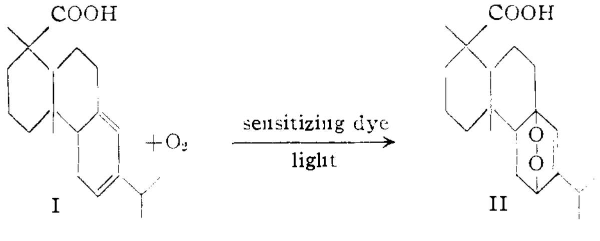
Levopimaric acid was found to add readily one mole of oxygen upon exposure of its alcoholic solution, containing a suitable sensitizing dye, to air and visible light. The oxidation product was characterized as a crystalline peroxide which contained no new Grignard-reactive hydrogen and showed no selective ultraviolet absorption between 220 and 320 mμ. The reaction rate was found to be independent of the resin acid concentration, directly proportional to the light exposure, and unaffected by the presence of hydroquinone. The peroxide is considered to be 6,14-peroxido-Δ7(8)-dihydroabietic acid.

This investigation was initiated to study the 1,4-addition of oxygen to the conjugated, homoannular, cyclohexadienic grouping in levopimaric acid, by the photosensitized process which has been applied to this type of compound in other fields. The production of a crystalline peroxide by irradiation and aeration of an alcoholic solution containing a diene and a sensitizing dye was first encountered with ergosterol[2] in connection with work on vitamin D. A variety of substituted 1,3-cyclohexadienes have since been shown to add oxygen under similar conditions. Among these are dehydroergosterol,[3] 2,4-cholestadiene,[4] α-terpinene,[5] α-phellandrene[5] and 1,3-cyclohexadiene.[5]

It was found that levopimaric acid (I) also readily added one mole of oxygen when irradiated in a suitable solvent containing a sensitizing dye. The product was characterized as a crystalline peroxide, m.p. 156–158° dec., $[\alpha]_D$ +101° (1.1% in ethanol), which showed no characteristic ultraviolet absorption between 220 and 320 mμ. The peroxide contained no new Grignard-reactive hydrogen, and the infrared spectrum of its methyl ester exhibited no O–H stretching band in the region of 3 μ. Elemental analyses and the neutralization equivalent also supported a tentative formulation of the peroxide as the expected 1,4-addition product, 6,14-peroxido-Δ7(8)-dihydroabietic acid (II).



The ease with which levopimaric acid is oxidized and isomerized in the presence of light and air has been pointed out elsewhere.[6] The autocatalytic air oxidation of levopimaric acid, involving a free radical chain type of reaction, results in a very complex mixture of oxidation products. Abstraction of hydrogen from the several activated positions open to oxidative attack leads to resonating systems which are subject to the addition of oxygen at a still larger number of positions. This would necessarily produce a complex product, without the additional factor of secondary reactions. The ultraviolet spectrum of autoxidized levopimaric acid was quite similar to the spectrum of thermally isomerized levopimaric acid. This was true even when the autocatalytic oxidation was conducted under conditions of temperature and acidity which do not normally cause the isomerization of levopimaric acid. Fortunately, the polar solvent and low temperature employed for the photo-sensitized air oxidation reported here are not conducive to free radical formation. Alcoholic solutions of levopimaric acid can be aerated and irradiated with visible light in the absence of sensitizing dyes for many hours without effecting a detectable change in the resin acid. The presence of hydroquinone did not affect the rate of the photo-sensitized reaction.

Side reactions occur if there is a deficiency of oxygen in the solvent during the oxidation. Under a nitrogen atmosphere, irradiation of a solution of levopimaric acid and sensitizer gave a product having an ultraviolet spectrum similar to the spectrum of rosin. The alteration of the resin acid was accompanied by a bleaching of the sensitizer and was possibly analogous to the formation of bis-ergostadienol from ergosterol under similar conditions.[7]

The oxidation of levopimaric acid under mild conditions in solution did not occur in the absence of light or a sensitizing dye. A number of dyes were tested for sensitizing activity. All of the resorcinolphthalein type dyes and methylene blue were effective sensitizers, whereas several other dyes such as thymol blue, crystal violet, rosaniline and phenolphthalein type dyes showed no activity. The structural feature absent in the inactive dyes and present in the active ones was the *o*-quinonoid grouping. Tests showed that two simple *o*-quinones, retenequinone and 1,2-naphthoquinone, were effective sensitizers, although unlike the other active compounds, they were gradually decolorized and deactivated during the oxidation process. The relative efficiencies of the various sensitizers, shown in Table I, are valid only under the experimental conditions, since these apparent efficiencies are dependent upon the spectrum of the light source and the transmittancy of the solvent and reaction vessel as well as their quantum efficiencies.

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[1] One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

[2] A. Windaus and J. Brunken, *Ann.*, **460**, 225 (1928).

[3] A. Windaus and L. Tinsert, *ibid.*, **465**, 157 (1928).

[4] E. Skau and W. Bergmann, *J. Org. Chem.*, **3**, 166 (1938); W. Bergmann, F. Hirschmann and E. Skau, *ibid.*, **4**, 29 (1939).

[5] G. O. Schenck and K. Ziegler, *Naturwissenschaften*, **32**, 157 (1944); **38**, 356 (1951).

[6] G. Dupont, *Compt. rend.*, **172**, 923 (1921).

[7] A. Windaus and P. Borgeaud, *Ann.*, **460**, 235 (1928); A. Windaus and O. Linsert, *ibid.*, **465**, 148 (1928); H. H. Inhoffen, *ibid.*, **497**, 130 (1932); R. P. Jacobsen and C. Z. Nawrocki, THIS JOURNAL, **62**, 2612 (1940).

TABLE I

Sensitizing dye[a]	Time required for complete reaction, hr.
Rose bengal	3.5
Methylene blue	4.5
Erythrosin	4.8
Eosin	7.7
Chlorophyll	72
2,5-Dimethyl-*p*-quinone	100

[a] Thymol blue, crystal violet, rosaniline, phenolphthalein, and halogenated phenolphthaleins showed no activity.

The reaction proceeded at the same rate in methyl, ethyl, isopropyl and *n*-butyl alcohols. It took place more slowly in acetone and not at all in heptane or benzene.

The reaction rate was independent of the concentration of levopimaric acid, and directly proportional to the light exposure.

Experimental

Levopimaric acid employed in these experiments was prepared from commericial pine gum by a modification[8] of the amine salt technique of Harris.[9]

Apparatus.—Three different types of apparatus were employed for the various stages and scales of oxidation reactions: 1. Preliminary experiments were conducted in a 500-ml., cylindrical, Pyrex, gas washing bottle equipped with a sintered-glass bottom suitable for the dispersion of oxygen in the reaction solution. The daylight fluorescent tube was found to be the more effective light source with the sensitizers employed.

2. Larger scale oxidations were conducted in an apparatus which consisted of two Pyrex tubes mounted vertically, one inside the other. The outer tube (7.5 cm. i.d. and 125 cm. in length) was fitted at its lower end with a sintered glass plate for gas input. The inner tube (4.5 cm. o.d. and 130 cm. long), open only at its upper end, contained a 40-watt fluorescent tube (Sylvania daylight). The reaction solution was charged to the outer tube so as to be illuminated from within.

Medium scale oxidations were conducted in a similar apparatus constructed of an outer tube (4.28 cm. i.d. and 54 cm. in length) and an inner tube (3.48 cm. o.d. and 55 cm. long), containing a 15-watt fluorescent tube (Westinghouse daylight).

3. Small scale oxidations and the study of variables were conducted in a set of four test-tubes, each 2.85 cm. in outside diameter and 26 cm. in length. Each tube was fitted with a reflux condenser and a sintered-glass, pencil-type, gas inlet extending almost to the bottom of the tube. Each tube was masked with opaque paper so that only a cylindrical, center, section, 140 mm. long, was exposed to light. The tubes were mounted vertically in a plane and irradiated by a 15-watt daylight fluorescent tube which was mounted horizontally in front of the centers of the tubes. In a preliminary test of the apparatus, 100-ml. samples of 0.02 *M* levopimaric acid in 95% ethanol, containing eosin (50 mg./l.), were sparged with oxygen and irradiated with a 200-watt incandescent lamp. The rate of change in $[\alpha]_D$ in a quadruplicate run, was +22.5 ± 0.5°/hr. The 15-watt fluorescent tube gave a better light distribution and a more rapid reaction, $\Delta[\alpha]_D$ +52.2°/hr. It was therefore used in subsequent determinations.

Light Exposure.—The incidence of light on the four tubes described under apparatus 3 above, was vertically symmetrical about the midpoint of the unmasked portion of the tubes. Tube 1 was completely masked so that no light could enter; tube 2 was masked from its midpoint up, so that 50% of the standard light exposure was obtained; tube 3 was left with a 140 mm. vertical section to receive a 100% light exposure. Three 100-ml. portions of 0.02 *M* levopimaric acid in 95% ethanol which contained 50 mg./l. of eosin, were irradiated and sparged with oxygen simultaneously. During this treatment, the solutions in each tube exhibited a rate of change of optical rotation proportional to the amount of incident light: Δ $[\alpha]_D$ tube 1, 0°/hr.; tube 2, +25.5°/hr.; tube 3, +52.2°/hr.

Effect of Alkali.—The test-tubes of apparatus 3 were charged with 100 ml. of solutions, each containing 0.002 mole of levopimaric acid and 5 mg. of eosin, and also in (1) no alkali, in (2) 0.001 mole of sodium hydroxide in (3) 0.002 mole of sodium hydroxide, and in (4) 0.003 mole of sodium hydroxide.

The changes in $[\alpha]_D$ during irradiation and oxidation were; for (1), +47°/hr.; (2), +46°/hr.; (3), +46°/hr.; and for (4), +42°/hr. In tube 4 the rate of change deviated from linearity after about 50% reaction and passed through a positive maximum of $[\alpha]_D$ +70°, after which the rotation decreased to +27° and became constant. The secondary reaction which occurred in the presence of excess alkali, is the subject of further study.

Sensitizers.—A number of dyes were tested for sensitizing activity at a level of 50 mg./l. in 0.02 *M* levopimaric acid solution in 95% ethanol. The reaction rates were determined by change in optical rotation where the solutions transmitted sodium light, and by changes in ultraviolet absorption in other cases. The time required for complete oxidation of the levopimaric acid was measured as the time required to reach constant optical rotation or for complete destruction of the ultraviolet absorption maximum at 272 mμ. The results are given in Table I.

Oxygen Absorption.—A solution comprised of 0.2444 g. of levopimaric acid and 2.0 mg. of eosin in 20 ml. of 95% ethanol was placed in a 50-ml. erlenmeyer flask fitted to a gas buret. The system was flushed and filled with oxygen. The solution was stirred magnetically while being irradiated with a 15-watt fluorescent light. Oxygen absorption was complete in 3 hr., but agitation and irradiation were continued for 4.5 hr. The sample absorbed 19.3 ml. of oxygen at 26° and 765 mm. pressure which amounts to 0.98 mole of oxygen/mole of levopimaric acid.

Air *vs.* Oxygen.—The four tubes of apparatus 3 were arranged so that alternate tubes were sparged with air and pure oxygen. Oxidation of quadruplicate samples of 0.02 *M* levopimaric acid in 95% ethanol sensitized by eosin (50 mg./l.) showed no significant difference in reaction rates among the tubes.

6,14-Peroxido-Δ7(8)-dihydroabietic Acid (II).—A solution comprised of 0.06 mole of sodium levopimarate and 25 mg. of methylene blue in sufficient 95% ethanol to give a volume of 400 ml. was charged to apparatus 1 and aerated and irradiated by a 200-watt incandescent lamp. The reaction temperature was in the range of 25 to 55°. The disappearance of the levopimaric acid was followed by the determination of ultraviolet absorption. The rate of disappearance was linear with respect to reaction time. After 25.3 hr., only 3.5% of the levopimaric acid remained unchanged. Aeration and irradiation were continued for 3.7 additional hours before termination. The oxidate solution was distilled until only a small volume remained. The residue was diluted with water, extracted with ether, acidified with acetic acid, and re-extracted with ether. The ether was removed from the latter extract by distillation. The oxidation product was dissolved in 50 ml. of 95% ethanol prior to the precipitation of the peroxide by the addition of 6 ml. of 2-amino-2-methyl-1-propanol. The amine salt, after two recrystallizations from ethanol, was obtained as white needles, 9.60 g., $[\alpha]^{25}_D$ +77.1° (1.16% in ethanol). The amine salt was slurried in ether and washed successively with 3 *N* acetic acid, water, 0.01 *M* sodium bicarbonate and water. The ether was removed from the salt by evaporation to give a residue which was crystallized from a mixture of alcohol and water. The final yield was 6.15 g. (33%) of fine white needles, m.p. 156–158° dec., $[\alpha]^{25}_D$ +101° (1.1% in ethanol).

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04; neut. equiv., 334. Found: C, 71.99; H, 9.10; neut. equiv., 334.

The peroxide liberated 1.10 moles of methane/mole of peroxide in a micro modification of the Zerewitinoff determination of active hydrogen. It showed no characteristic absorption of ultraviolet light in the 220 to 320 mμ range.

Methyl 6,14-Peroxido-Δ7(8)dihydroabietate.—An ethereal solution containing 2.0 g. of the above peroxide was treated with a slight excess of an ethereal solution of diazomethane. The ether and excess diazomethane were removed by distillation and the residue was recrystallized from methanol to give 1.3 g. of the methyl ester, m.p. 96–98°. After two additional recrystallizations from methanol, the

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[8] V. M. Loeblich, D. E. Baldwin, R. T. O'Connor and R. V. Lawrence, THIS JOURNAL, **77**, 6311 (1955).

[9] G. C. Harris and T. F. Sanderson, *ibid.*, **70**, 334 (1948).

ester (1.00 g.) melted at 100–101°, and remelted at 99.5–100.5°, $[\alpha]_D$ +93.5° (2% in ethanol). No O–H stretching band was observed in the region of 3 μ in its infrared spectrum.

Anal. Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.55; H, 9.38.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TEXAS SOUTHERN UNIVERSITY]

Some Further Reactions of 2,6-Dimethyl-4-pyrone

BY L. L. WOODS

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Continuing the investigation of the fundamental chemical nature of the mononuclear 4-pyrones, we are reporting two new reactions of 2,6-dimethylpyrone and an expansion of a previously published[1] reaction on the same compound.

Boon[2] and co-workers have been able to condense aromatic aldehydes with the methyl groups of 2,6-dimethyl-4-pyrone to give bis-(arylmethylenes) and efforts in this Laboratory to adapt the method to produce mono-(arylmethylenes) failed.

The condensation of aldehydes with methylated polynuclear 4-pyrones reported by Schönberg[3] and his co-workers failed with 2,6-dimethyl-4-pyrone, the aldehyde always being recovered.

Good yields of mono-(arylmethylene) derivatives of 2,6-dimethyl-4-pyrone were finally obtained simply and in good yield using potassium hydroxide as the condensing agent (Table I).

Chlorination of the mono-(arylmethylene) derivatives with sulfuryl chloride caused addition of two atoms of chlorine except with Id from piperonal which gave a trichloride by concurrent addition and substitution.

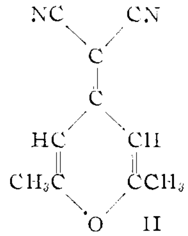
The recent publication of Mustafa[4] in which the condensation of two molecules of polynuclear 2-aryl-1,3-benzoxaz-4-thiones was reported, suggested the reaction of malononitrile with 2,6-dimethyl-4-pyrone which gave 4-(dicyanomethylene)-4H-pyran (II) in excellent yield.

Malononitrile was selected in preference to other compounds with active methylenes to remove the oxygen of the pyrone carbonyl since it does not react with acetic anhydride, or with any group of the dimethylpyrone other than the carbonyl oxygen. The nitrile thus produced is easily hydrolyzed to the dibasic acid, characterized by the diphenacyl derivative.

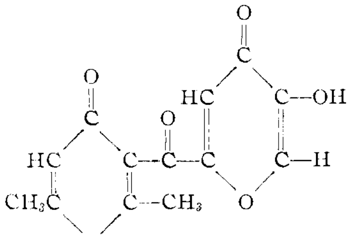
In a previous publication[1] the acylation of 2,6-dimethyl-4-pyrone with an aromatic acid in the presence of zinc chloride at the temperature of boiling xylene was described. This reaction has been extended to produce a few derived pyrones (IIIa-d). With succinic acid, cyclization rather than diketone formation occurred to yield a furan (IIIb). The diketone from levulinic acid also reacted further to give IIIc, a cyclic ketone containing a 7-membered ring.

The pyrone carbonyl of 2,6-dimethyl-4-pyrone and of compounds IIIb, IIIc and IIId is unaffected by potassium borohydride, but the expected reduction of the reactive carbonyl of the last three occurred. 2,6-Dimethyl-3-comenyl-4-pyrone (IIIa) failed to give a recognizable product.

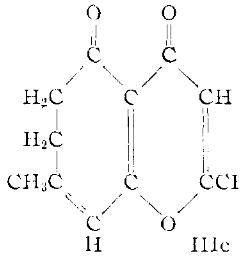
Infrared data are given for compounds II, IIIa and IIIc.



II



IIIa



IIIc

Experimental[5]

Preparation of Compounds Ia–d.—A solution of 2 g. of potassium hydroxide in 50 ml. of absolute methanol was treated with 0.05 mole (6.2 g.) 2,6-dimethyl-4-pyrone and 0.05 mole of the aldehyde and allowed to stand at room temperature for 24 hours. The solid or semi-solid, was broken up, poured into 250 ml. of water containing 10 ml. of concentrated hydrochloric acid and the precipitated material was collected, air-dried then recrystallized from absolute ethanol. Physical properties and analytical data for this series are given in Table I.

Chloro Derivatives of Ia–d.—One gram of the crude compound was treated with 5 ml. of sulfuryl chloride at room temperature. The vigorous reaction was complete within 10 minutes and the complex was then broken up by adding 50 ml. of water. The yellow or orange solid was collected, dried in air, and recrystallized from absolute ethanol (boiling heptane with the chloro derivative of Id). Table II contains physical properties and analytical data for this series.

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[1] L. L. Woods, *J. Org. Chem.*, **22**, 341 (1957).

[2] A. A. Boon, K. J. McKinzie and J. Trotter, *Proc. Chem. Soc.*, **30**, 205 (1914).

[3] (a) A. Schönberg, M. M. Sidky and G. Aziz, THIS JOURNAL, **76**, 5115 (1954); (b) A. Schönberg, A. E. K. Fateen and E. M. A. Sammour, *ibid.*, **78**, 4689 (1956).

[4] Ahmed Mustafa and A. E. A. A. Hassin, *ibid.*, **79**, 3846 (1957).

[5] All analyses and molecular weight determinations were made by Dr. Carl Tiedcke. Melting points were taken on a Fisher-Johns melting point assembly.