[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

An Intramolecular Rearrangement of 4-Benzoyloxycyclohexanone

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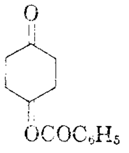
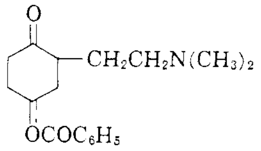
Attempted alkylation of 4-benzoyloxycyclohexanone (I) in the 2-position with 2-dimethylaminoethyl chloride in the presence of sodamide yielded 2-dimethylaminoethyl 2′-benzoylcyclopropanepropionate (VIb). Treatment of I with sodamide alone yielded 4-hydroxy-7-oxo-7-phenylheptanoic acid γ-lactone (V) and 2-benzoylcyclopropanepropionic acid (VIa).

The recent announcement by Yates and Anderson[1] of the base-catalyzed rearrangement of 4-benzoyloxycyclohexanone to 2-benzoylcyclopropanepropionic acid prompts us to report our findings concerning this rearrangement.

In the course of our research, we attempted to prepare 4-benzoyloxy-2-(2′-dimethylaminoethyl)-cyclohexanone (II) by the alkylation of 4-benzoyloxycyclohexanone (I) with 2-dimethylaminoethyl chloride in the presence of sodamide. The product of this reaction was a stable, distillable liquid which yielded a crystalline hydrochloride salt. It was produced in 39% yield when the reaction was run in boiling toluene for 24 hours using two moles of dimethylaminoethyl chloride per mole of ketoester. Lesser reaction times and/or the use of benzene as a solvent lowered the yield. Xylene as a solvent offered no advantage. Elemental analysis of the product was satisfactory for compound II but, unexpectedly, it lost nitrogen upon alkaline hydrolysis. Our study of the hydrolysis products, confirmed by the findings of Yates and Anderson in their excellent work,[1] revealed the nature of the "alkylated" material.



I



II

Hydrolysis of the "alkylated" material with aqueous alcoholic sodium hydroxide led to the isolation of a lactone, m.p. 76-77.5° (6% yield) and a carboxylic acid, m.p. 66.5-68.5° (61% yield) (see below). The lactone ($C_{13}H_{14}O_3$) yielded benzoic acid upon treatment with alkaline permanganate and showed $\lambda_{\max}^{CS_2}$ 5.61 (γ-lactone) and 5.91 μ (benzoyl), $\lambda_{\max}^{EtOH}$ 243 mμ (ε 12,700) and 278 mμ (ε 1,050). Its structure was postulated as 4-hydroxy-7-oxo-7-phenylheptanoic acid γ-lactone (V) and the postulate was then confirmed by an unequivocal synthesis.

This was accomplished starting with diethyl γ-oxopimelate.[2] Catalytic reduction of the latter ketoester afforded γ-hydroxypimelic acid ethyl ester γ-lactone (87%) which, upon alkaline hydrolysis and acidification, furnished γ-hydroxypimelic acid γ-lactone (68%). Treatment of the lactone-acid with thionyl chloride yielded γ-hydroxypimelic acid chloride γ-lactone (80%) which, in turn, reacted with phenylcadmium to produce compound V. The samples of V from the two sources were identical. The 2,4-dinitrophenylhydrazone of V melted at 176.4-178.4°.

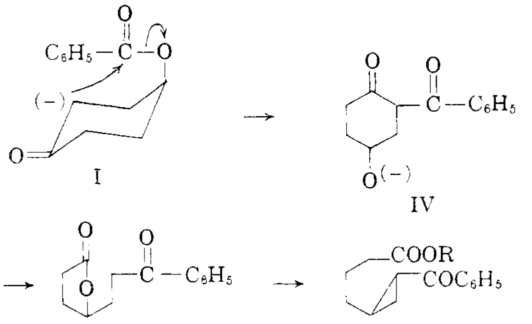
The acidic product of m.p. 66.5-68.5°, isolated in 61% yield from the above-mentioned hydrolysis, was isomeric with V and also yielded benzoic acid upon treatment with alkaline permanganate. It showed $\lambda_{\max}^{EtOH}$ 243 mμ (ε 15,500) and 278 mμ (ε 1,100). It was convertible to an amide, m.p. 127.8-128.6°, $\lambda_{\max}^{EtOH}$ 243mμ (ε 15,800) and 278 mμ (ε 1,000). The oxygen in the acid was accounted for by the –COOH and C_6H_5CO– groups. The remaining C_5H_8 fragment was either unsaturated or cyclical.

Hydrogenation of both the acid and the amide in the presence of palladium-on-charcoal resulted in absorption of three moles of hydrogen (two moles to reduce the aroyl carbonyl group) but gave mixtures from which no pure compounds were isolated. The original postulation that the acid was 7-oxo-7-phenyl-5-heptenoic acid (III) was discounted by the failure to isolate 7-phenylheptanoic acid and 7-phenylheptanamide after the above hydrogenations.

$$C_6H_5COCH{=}CH(CH_2)_3COOH$$

III

A ring structure capable of hydrogenolysis, *i.e.*, cyclopropane, seemed to be required by the data. The acid was tentatively identified as 2-benzoylcyclopropanepropionic acid (VIa). Yates and Anderson have substantiated this structure.



VIa, R = H
VIb, R = $-CH_2CH_2N(CH_3)_2$

Isolation of the γ-lactone V led us to envision the first stage of the "alkylation" reaction as an intramolecular ester condensation (I→IV) related to the Baker–Venkataraman rearrangement[3,4] wherein *o*-(acyloxy)-acetoarones yield *o*-hydroxy-α-acylacetoarones in the presence of strong bases. Intramolecular attack by the anionic center shown in formula IV on the carbonyl group of the ring (with simultaneous ring cleavage) should be the source of

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[1] Peter Yates and Charles D. Anderson, THIS JOURNAL, **80**, 1264 (1958).

[2] W. Marckwald, *Ber.*, **20**, 2813 (1887).

[3] Wilson Baker, *J. Chem. Soc.*, 1381 (1933).

[4] H. S. Mahal and K. Venkataraman, *Current Sci.*, **2**, 214 (1933).

the γ-lactone V. Indeed, when 4-benzoyloxycyclohexanone was treated with sodamide in boiling benzene without the aminoalkyl chloride, the products isolated were the lactone V (4.5%) and the acid VIa (31)%. Yates and Anderson[1] have demonstrated the transformation of V[5] to VIa and have suggested that IV and V are intermediates in the conversion of I to VIa. The acid VIa, as its sodium salt, immediately becomes available for reaction with the 2-dimethylaminoethyl chloride present in the system first described.

Our "alkylated" material was, therefore, 2-dimethylaminoethyl 2′-benzoylcyclopropane-propionate (VIb). It showed the expected $\lambda^{\mathrm{CS_2}}_{\mathrm{max}}$ 5.75 (ester) and 5.98 μ (benzoyl), $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ 243 mμ (ε 14,000) and 278 mμ (ε 920). The γ-lactone V found after the hydrolysis of the ester VIb apparently was present as a contaminant in the sample of ester. The latter (free base) showed a very weak infrared band at 5.61 μ which is characteristic of the γ-lactone and indicated its presence.

Experimental[6]

2-Dimethylaminoethyl 2′-Benzoylcyclopropanepropionate (VIb).—To a stirred, refluxing solution of 20.0 g. (0.092 mole) of 4-benzoyloxycyclohexanone[7] (I) in 100 ml. of toluene was added, in one portion, 58 ml. of a 3.13 molar solution of 2-dimethylaminoethyl chloride in toluene (0.184 mole of halide) and then 3.6 g. (0.092 mole) of sodamide. The mixture was refluxed for 20 hours, cooled, and treated with 50 ml. of water. The organic layer was extracted with dilute hydrochloric acid and the product liberated from this extract by basification. When taken up in ether, dried (K_2CO_3) and freed from ether, the product (12.0 g.) distilled at 155–165° (0.05 mm.). Redistillation gave 10.5 g. (39%), b.p. 165–168° (0.2 mm.), $n^{25}\mathrm{D}$ 1.5198.

Anal. Calcd. for $C_{17}H_{23}NO_3$: C, 70.55; H, 8.01; N, 4.84. Found: C, 70.56; H, 7.91; N, 4.93.

The hydrochloride salt of this base was prepared as colorless, hygroscopic crystals from ethyl acetate–hexane, m.p. 79.5–81.5°.

Anal. Calcd. for $C_{17}H_{24}ClNO_3$: C, 62.65; H, 7.42; Cl, 10.87. Found: C, 62.41; H, 7.64; Cl, 10.87.

Hydrolysis of 2-Dimethylaminoethyl 2′-Benzoylcyclopropanepropionate (VIb).—A solution of 30 g. (0.104 mole) of VIb in 60 ml. of ethanol was added to 13.5 g. (0.34 mole) of sodium hydroxide dissolved in 40 ml. of water and the mixture was refluxed for one hour. The solvent was removed by warming *in vacuo*, the residue was partitioned between water and ether, and the water layer was acidified with concentrated hydrochloric acid. The liberated oil was extracted with ether and dried (Na_2SO_4) solution (800 ml.) was diluted with 1200 ml. of pentane. This solution was chromatographed on 500 g. of silica gel. **2-Benzoylcyclopropanepropionic acid (VIa)** was eluted first. After recrystallization from a mixture of 200 ml. of hexane and 75 ml. of benzene, it melted at 66.5–68.5° (13.9 g., 61%).[8]

Elution with 4:1 ether–pentane removed **4-hydroxy-7-oxo-7-phenylheptanoic acid γ-lactone (V)** which, after recrystallization from ethanol, melted at 76–77.5° (1.45 g., 6.4%).[8]

γ-Hydroxypimelic Acid Ethyl Ester γ-Lactone.—A solution of 33 g. (0.14 mole) of diethyl γ-oxopimelate[2] in 200 ml. of absolute alcohol was subjected to hydrogen under 300 lb. pressure in the presence of Raney nickel at 75° for 6 hours. The catalyst and solvent were removed and the residual oil distilled to give 23.1 g. (87%) of somewhat impure γ-hydroxypimelic acid ethyl ester γ-lactone, b.p. 134–136° (0.8 mm.), $n^{25}\mathrm{D}$ 1.4470.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.22; H, 8.25.

γ-Hydroxypimelic Acid γ-Lactone.—A mixture of 23.1 g. (0.125 mole) of γ-hydroxypimelic acid ethyl ester γ-lactone, 14 g. (0.25 mole) of potassium hydroxide, 100 ml. of water and 20 ml. of ethanol was heated under reflux for 7 hours, cooled and acidified with concentrated hydrochloric acid. The solution was concentrated to a paste by warming *in vacuo*, the residue was boiled with 1 l. of benzene and the mixture filtered. Concentration of the benzene solution to a 50-ml. volume and cooling gave 13.4 g. (68%) of γ-hydroxypimelic acid γ-lactone, m.p. 81–84°.

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.19; H, 6.66.

γ-Hydroxypimelic Acid Chloride γ-Lactone.—A mixture of 12 g. (0.076 mole) of γ-hydroxypimelic acid γ-lactone, 11.9 g. (0.1 mole) of thionyl chloride and 50 ml. of chloroform was heated under reflux for 2 hours, and then distilled. The product (10.7 g., 80%), boiled at 133–139° (0.1 mm.).

Anal. Calcd. for $C_7H_9ClO_3$: C, 47.60; H, 5.14; Cl, 20.08. Found: C, 47.95; H, 5.55; Cl, 19.75.

4-Hydroxy-7-oxo-7-phenylheptanoic Acid γ-Lactone (V).—To a cold, stirred solution of phenylmagnesium bromide prepared from 8.2 g. (0.052 mole) of bromobenzene and 1.27 g. (0.052 mole) of magnesium in 50 ml. of ether was added 9.54 g. (0.052 mole) of solid cadmium chloride portionwise in 30 minutes. The ice-bath was removed and the mixture stirred for one hour. To the mixture, again cooled in ice, was added dropwise 9.2 g. (0.052 mole) of γ-hydroxypimelic acid chloride lactone in 30 minutes, stirring was continued for 30 minutes, and the mixture was then treated with ice-water and finally with dilute hydrochloric acid. The ether layer was dried (Na_2SO_4) and the ether evaporated. Distillation of the residual oil separated, a few drops boiling at 44° (0.15 mm.). The residue, dissolved in ether and chilled several days, afforded a solid which, after two recrystallizations from aqueous ethanol, melted at 77–79° (0.3 g.). This melted at 76–79° when mixed with a sample, m.p. 76–77°, prepared from the reaction of 4-benzoyloxycyclohexanone with sodamide. The infrared spectra of the compounds were identical. Chromatography on 30 g. of silica gel using 1:1 ether–hexane for elution gave 0.25 g. of plates melting at 78–80°.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.70; H, 6.54.

The 2,4-dinitrophenylhydrazone of V melted at 176.4–178.4° (from ethanol).

Anal. Calcd. for $C_{19}H_{18}N_4O_6$: C, 57.28; H, 4.55; N, 14.06. Found: C, 57.68; H, 4.68; N, 14.50.

2-Benzoylcyclopropanepropionamide.—A 0.5-g. sample of 2-benzoylcyclopropanepropionic acid (VIa) was refluxed with 2.2 ml. of thionyl chloride for 15 minutes. The cooled mixture was poured into concentrated ammonium hydroxide and the precipitated solid filtered (0.35 g.). Three recrystallizations from ethyl acetate gave 0.11 g. of white needles, m.p. 127.8–128.6°; $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ 243 mμ (ε 15,800), 278 mμ (ε 1,000).

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.85; H, 6.96. Found: C, 71.66; H, 7.14.

Reaction of 4-Benzoyloxycyclohexanone with Sodamide.—A mixture of 46.8 g. (0.214 mole) of 4-benzoyloxycyclohexanone, 8.13 g. (0.214 mole) of sodamide and 200 ml. of dry benzene was warmed to initiate reaction (55–70°). After the spontaneous reaction subsided, the mixture was refluxed for one hour, cooled, and treated with cold water. The water layer was acidified, the precipitated oil taken up in ether, and the dried (Na_2SO_4) solution freed from solvent. The residual oil, in 1:1 ether–pentane, was chromatographed on 1 kg. of silica gel. The solvent mixture eluted a trace of benzoic acid and then 26 g. of 2-benzoylcyclopropanepropionic acid (VIa), m.p. 67–72°. Recrystallized from benzene–hexane, this acid melted at 70–73° (14.4 g., 31%), b.p. 170–171° (0.05 mm.), $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ 243 mμ (ε 15,500) and 278 (ε 1,100), $\lambda^{\mathrm{CS_2}}_{\mathrm{max}}$ 5.83 and 5.97 μ.

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[5] Synthesized from VIa but not isolated from the rearrangement reaction.

[6] All melting points are corrected. The 100–200 mesh silica gel used for chromatography was obtained from the Davison Chemical Corp., Baltimore, Md. The authors thank Mr. K. D. Fleischer and his associates for the analytical data reported and Miss Catherine Martini and Mrs. M. Becker for spectral determinations.

[7] E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 615 (1949).

[8] See the last preparation in the Experimental section for analytical and further physical data.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; neut. equiv., 218. Found: C, 71.45; H, 6.56; neut. equiv., 215.

Elution of the column with 10 l. of pure ether followed by 1:4 acetone-ether removed 4-hydroxy-7-oxo-7-phenylheptanoic acid γ-lactone (V) which crystallized from ethanol as massive orthorhombic prisms, m.p. 76–77° (2.2 g., 4.5%), b.p. approx. 165–170° (0.04 mm.), λ_{max}^{EtOH} 243 mμ (ε 12,700) and 278 mμ (ε 1,050), $\lambda_{max}^{CS_2}$ 5.61 and 5.91 μ.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47; sapon. equiv., 218. Found: C, 71.57; H, 6.43; sapon. equiv., 213.

RENSSELAER, N. Y.

[CONTRIBUTION NO. 470 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO.]

Polymeric Peroxide of 1,3-Butadiene

BY C. T. HANDY AND H. S. ROTHROCK

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Controlled peroxidation of butadiene solutions has been found to produce, in high yield, polymer of molecular weight 700–850 comprising vinylethylenedioxy and 2-butenylenedioxy units (equation 1). This polymer is formed by both 1,2- and 1,4-addition of oxygen to butadiene, with 1,4-addition predominating. Structural confirmation was obtained by reduction to the corresponding butenediols and butanediols.

Although the formation of polymeric peroxides from several related dienes has been reported,[1–4] no detailed study of the peroxidation of 1,3-butadiene appears to have been made. A published reference to a peroxide of this diene describes only an extremely explosive product.[5] It has now been found that a relatively stable polymeric peroxide can be prepared in high yield by the controlled oxidation of butadiene in solution. This paper describes this synthesis and the characterization of the peroxide.

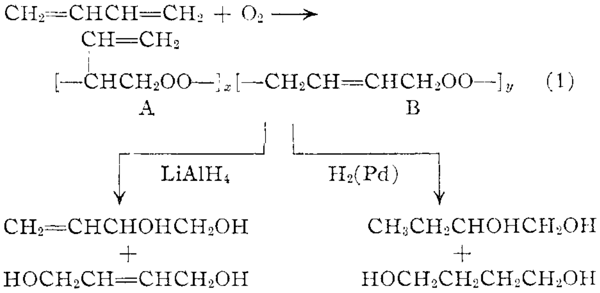
When the reaction of butadiene and oxygen was carried out in the presence of a suitable solvent at 85–95° and was stopped before more than about 50% of the butadiene had reacted, a liquid peroxide was obtained. The reaction temperature appeared quite critical; reaction below 75° was impractically slow, whereas above 95° secondary reactions took place yielding benzene-insoluble products. The peroxidation followed a typical autocatalytic curve and exhibited a pronounced induction period which could be minimized by the addition of a source of free radicals. The rate of oxidation showed dependence on the concentration of butadiene, but not on oxygen pressure.

Benzene was the best of the solvents tested; dioxane and 1,1,1-trichloroethane also were satisfactory. Acidic media inhibited the peroxidation, and bases caused destruction of peroxide.

The stability of the peroxide of butadiene is much greater than was expected. Benzene solutions have been stored at 25° for several weeks without significant decomposition. At 100° the solutions had a half-life of about 13 hr. However, in concentrated form the peroxide can be detonated by ignition or severe shock and appropriate precautions must be observed in its handling. A satisfactory method for decomposition of peroxidic residues involves treatment with strong aqueous caustic.

The peroxide obtained by careful evaporation of solvent under reduced pressures was a pale yellow, slightly viscous oil ($n^{25}D$ 1.5052). It was readily soluble in acetone, dioxane and chloroform, sparingly soluble in methanol and ether, and insoluble in water. Analyses established an approximate empirical formula $C_4H_6O_2$ and a polymeric structure having 8–10 units. Since iodometry[6] established that all of the oxygen was present as peroxide, this product must then be an alternating copolymer of butadiene and oxygen.

The points of attachment of the peroxy links were fixed by reduction experiments. Treatment with lithium aluminum hydride gave *trans*-2-butene-1,4-diol and 3-butene-1,2-diol as the only isolable products; catalytic hydrogenation gave the corresponding butanediols. The 1,4-diols predominated, in contrast with work[4] on peroxides of 2,3-dimethyl-1,3-butadiene in which no 1,4-diols were isolated. Thus, both 1,2- and 1,4-addition of oxygen to butadiene must have occurred.



$$CH_2{=}CHCH{=}CH_2 + O_2 \longrightarrow \underset{A}{[-\overset{\overset{\displaystyle CH{=}CH_2}{|}}{C}HCH_2OO-]_x}\underset{B}{[-CH_2CH{=}CHCH_2OO-]_y} \quad (1)$$

$$\xrightarrow{LiAlH_4} CH_2{=}CHCHOHCH_2OH + HOCH_2CH{=}CHCH_2OH$$

$$\xrightarrow{H_2(Pd)} CH_3CH_2CHOHCH_2OH + HOCH_2CH_2CH_2CH_2OH$$

The infrared absorption pattern for butadiene peroxide is in agreement with this assignment. Other reactions obtained with the peroxide can be explained on the basis of this copolymer structure. Thus thermal decomposition of unit structure A should involve C–C scission with formation of acrolein and formaldehyde, and these compounds have been isolated among the products of pyrolysis of butadiene peroxide to an extent equivalent to

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[1] K. Bodendorf, *Arch. Pharm.*, **271**, 1 (1933).

[2] E. H. Farmer, *Trans. Faraday Soc.*, **42**, 228 (1946).

[3] (a) W. Kern, H. Jockusch and A. Wolfram, *Makromol. Chem.*, **3**, 223 (1949); (b) W. Kern and J. Stallmann, *ibid.*, **7**, 199 (1951).

[4] F. K. Kawahara, THIS JOURNAL, **79**, 1447 (1957).

[5] D. A. Scott, *Chem. Eng. News*, **18**, 404 (1940).

[6] In common with peroxides of other conjugated dienes[7] the peroxide of butadiene does not respond satisfactorily to conventional iodometric procedures. The procedure adopted, involving a digestion with an acetic acid solution of hydroiodic acid at 60°, gave reproducible results with both butadiene peroxide and *t*-butyl peroxide.

[7] C. D. Wagner, R. H. Smith and E. D. Peters, *Ind. Eng. Chem., Anal. Ed.*, **19**, 976 (1947).