284 mμ, E_{mol} 13,750; reported[5] $\lambda_{\max}^{\text{alc}}$ 284 mμ, E_{mol} 26,300. Thus, a yield of 52% was indicated.[16]

The above procedure was repeated for *o*-quinone, 1,2-naphthoquinone and 1,4-naphthoquinone. With *o*-quinone there was no absorption in the ultraviolet (215–300 mμ) and the material recovered was shown to be cholesterol by melting point and the lack of depression in a mixture melting point. The total crude from 1,2-naphthoquinone had an absorption maximum at $\lambda_{\max}^{\text{alc}}$ 239 mμ,[17] E_{mol} 9300, and no absorption at 284 mμ. In the case of 1,4-naphthoquinone the total crude exhibited absorption at $\lambda_{\max}^{\text{alc}}$ 284 mμ, E_{mol} 6200.

Attempted Oxidation of Cholesterol and Δ^5-Cholestene-3-one Ethylene Ketal in the Absence of Aluminum Isopropoxide.—The above experiment was repeated on both cholesterol and Δ^5-cholestene-3-one ethylene ketal except the addition of aluminum isopropoxide was omitted. In both cases the ultraviolet analysis indicated the lack of diene system (215–300 mμ) and the starting materials were recovered unchanged.

Reaction of $\Delta^{3,5}$-3-Acetoxycholestadiene with *p*-Quinone. a. **In the Absence of Acid Catalyst.**—Two hundred mg. of $\Delta^{3,5}$-3-acetoxycholestadiene was heated in 15 ml. of dry toluene for four hours with 1.2 g. of *p*-quinone. The quinone was washed out of the reaction mixture as described above and, after concentration of the organic layer under reduced pressure, the ultraviolet absorption spectrum (215–300 mμ) run in absolute alcohol on the total crude material; $\lambda_{\max}^{\text{alc}}$ 235 mμ, E_{mol} 18,500, no absorption in the 284 mμ region.

b. **In the Presence of an Acid Catalyst.**—Two hundred mg. of $\Delta^{3,5}$-3-acetoxycholestadiene, 1.2 g. of *p*-quinone and 100 mg. of anhydrous aluminum chloride were refluxed 45 minutes in 15 ml. of dry toluene. The reaction mixture was worked up as described above in the Wettstein–Oppenauer oxidation of cholesterol and the ultraviolet absorption spectrum (215–300 mμ) was run in absolute alcohol on the total crude material; $\lambda_{\max}^{\text{alc}}$ 235 mμ, E_{mol} 10,400; $\lambda_{\max}^{\text{alc}}$ 284 mμ, E_{mol} 11,600.

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(16) Small amounts of the quinones used, in the total crude product, would not interfere with this determination, since none of their absorption maxima, given below, appear in the 284 mμ region where $\Delta^{4,6}$-3-keto-steroids absorb. *p*-Quinone: $\lambda_{\max}$ 210, 220, 232 and 243 mμ, all having log E_{mol} *ca.* 1.3; λ_{inf} 330 mμ, log E 2.5; $\lambda_{\max}$ 410 mμ, log E 4.4 (L. C. Anderson and M. B. Geiger, This Journal, **54**, 3064 (1932)). 1,2-Naphthoquinone: $\lambda_{\max}^{\text{alc}}$ 250 mμ, log E 4.4; $\lambda_{\max}^{\text{alc}}$ 340 mμ, log E 3.4, $\lambda_{\max}^{\text{alc}}$ 405 mμ, log E 3.4 (S. Goldschmidt and F. Graef, *Ber.*, **61**, 1858 (1928)). 1,4-Naphthoquinone: $\lambda_{\max}^{\text{alc}}$ 246 mμ, log E 4.37; $\lambda_{\max}^{\text{alc}}$ 330 mμ, log E 3.44 (R. A. Morton and W. T. Earlam, *J. Chem. Soc.*, 159 (1941)).

(17) This is in good agreement for Δ^4-3-ketocholestenone; L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 190.

[Contribution from the Laboratory of Chemistry of Natural Products, National Heart Institute, National Institutes of Health]

Reduction of Enols. New Synthesis of Certain Methoxybenzsuberenes via Hydrogenation of Dehydroacetic Acids

By Gordon N. Walker

Received January 18, 1956

Hydrogenation of dehydroacetic acid in the presence of 10% palladium–charcoal in ethyl acetate at 80° permits selective reduction of the acetyl group and affords 3-ethyl-4-hydroxy-6-methyl-5,6-dihydro-2-pyrone. Stepwise hydrogenation of veratrylidenedehydroacetic acid similarly affords 3-[γ-(3,4-dimethoxyphenyl)-propyl]-4-hydroxy-6-methyl-5,6-dihydro-2-pyrone, which is cyclized by polyphosphoric acid to 2,3-dimethoxy-5-(β-hydroxypropyl)-6-carboxybenzsuber-5-ene lactone. Evidence is presented confirming the structures of these and related products. *o*-Hydroxyacetophenone also may be reduced to *o*-ethylphenol by the same method.

A recent paper by Wiley and his students[1] showed that veratraldehyde and other aldehydes condense with the acetyl group of dehydroacetic acid and give chalcone-like compounds (III). This paper describes selective reduction of III and cyclization of the product (V) to a benzsuberene (VII).

Preliminary reduction studies were carried out with dehydroacetic acid (I). A method disclosed earlier[2] gave good results. It was found that compound I absorbed somewhat more than three moles of hydrogen in the presence of 10% palladium–charcoal in ethyl acetate at 80°. The crystalline product (56% yield) was the enolic keto-lactone II. Structure II was proven correct by hydrolysis and decarboxylation, which gave 2-hepten-4-one, and hydrogenation of this product, which led to formation of di-*n*-propyl ketone.

Experiments with veratrylidenedehydroacetic acid (III) which were carried out next, showed that it was possible, and in fact best, to reduce III in two stages. In the first stage, one mole of hydrogen was absorbed rapidly and the 3-[β-(3,4-dimethoxyphenyl)-propionyl]-pyrone (IV) was obtained in 86% yield. Structure IV was substantiated by similarity of the infrared spectra of IV and I in the carbonyl region, and by alkaline cleavage to β-(3,4-dimethoxyphenyl)-propionic acid. A mono-2,4-dinitrophenylhydrazone was prepared from IV. The infrared spectrum of this derivative showed that two carbonyl groups (5.80 and 5.87 μ) and conjugated unsaturation (6.07 μ) were present, as well as the usual N–H (3.02 μ) and C=N (6.17 μ) groups. The second reduction stage, from IV to V, involved absorption of three moles of hydrogen, as in reduction of I to II, and was slower than the first step. Compound V was obtained in 80% yield. The infrared spectrum of V in the carbonyl region was like that of II, having a double peak at 5.69 and 5.81 μ. Structure V was confirmed by cleavage with 5% alkali to ketone VI. In contrast to IV, compound V reacted very slowly with 2,4-dinitrophenylhydrazine. Evidently the 4-keto (or enol) group in I and IV is much less reactive than the acetyl group, an observation which is in keeping with properties of other cyclic 1,3-dicarbonyl compounds. The selective reduction of the acetyl sidechain in these compounds may depend upon this difference in char-

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(1) R. H. Wiley, C. H. Jarboe and H. G. Ellert, This Journal, **77**, 5102 (1955).

(2) G. N. Walker, *ibid.*, **77**, 3844, 6699 (1955).

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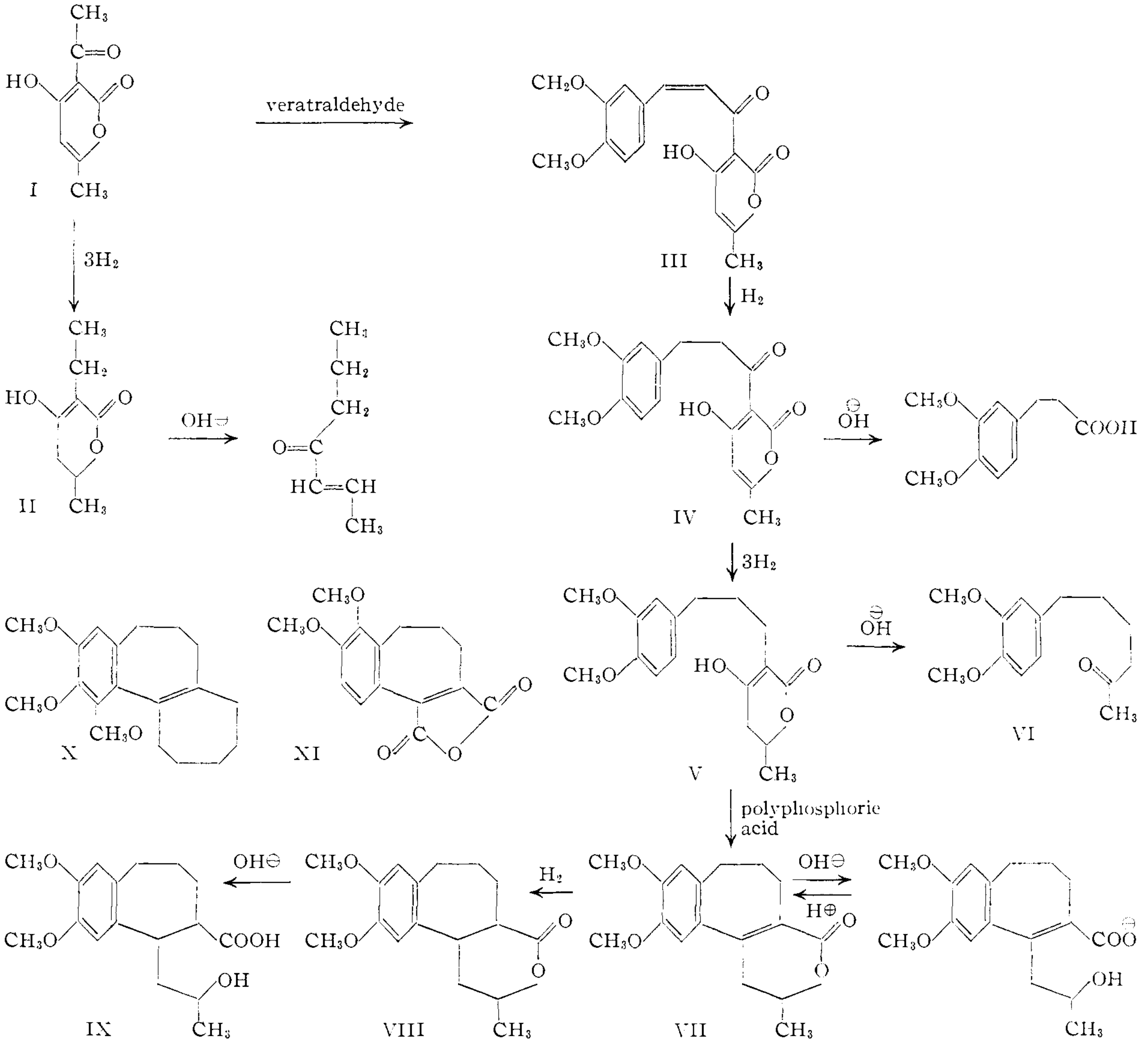

acter of the carbonyl groups, as well as upon other influences which are discussed later.

After some trial experiments it was found that keto-(or enol)-lactone V could be cyclized by means of polyphosphoric acid[3] at 85°. The reaction was slow and appeared to be accompanied by decomposition. A crystalline, neutral compound, $C_{17}H_{20}O_4$, m.p. 155–156°, was obtained in 14% yield. This product was the expected benzsuberene lactone VII, as will be evident from the following discussion. Compound V theoretically could also cyclize in another way, and some reaction of this kind actually may have occurred, since neutral, ketonic material also was isolated. However, no pure compounds were obtained from this fraction. Infrared (5.88–5.92 μ) and ultraviolet spectra (data in Experimental part) agreed with a conjugated, unsaturated lactone structure, and VII characteristically was reconstituted upon acidification of solutions of the sodium salt of the hydroxy acid. The latter compound could not be isolated. Hydrogenation of VII in the presence of palladium–charcoal at 80° gave the dihydro-lactone VIII. The corresponding δ-hydroxy acid IX was prepared by hydrolysis of VIII. The infrared spectrum of VIII had a peak at 5.80 μ, as expected for a saturated δ-lactone, and the ultraviolet spectrum (see Experimental part) pointed out disappearance of the conjugated lactone chromophore of VII. Compound X derived from colchicine is like VII in having a tetrasubstituted, conjugated double bond, and is reported[4] to resist hydrogenation. However, no difficulty was experienced in converting VII to VIII. This difference may be due to greater susceptibility of VII than X to hydrogenation or to greater efficacy of the method used here. Compound VIII is believed at present to have a *cis* B/C ring junction.

Lactone VII forms again more readily than does lactone VIII upon acidification of alkaline solutions of the respective hydroxy acids. This fact may be due to more favorable steric factors in the case of the unsaturated compound, and is in keep-

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(3) *Cf.* J. Koo, THIS JOURNAL, **75**, 720 (1953).

(4) H. Rapoport, A. R. Williams, J. E. Campion and D. E. Pack, *ibid.*, **76**, 3693 (1954).

ing with similar observations concerning the relative stabilities of benzsuberan-5,6-dicarboxylic and benzsuber-5-ene-5,6-dicarboxylic acid anhydrides.[5]

A previously unpublished synthesis[6] of 1,2-dimethoxybenzsuber-5-ene-5,6-dicarboxylic acid anhydride (XI) is included in the Experimental portion of this paper. It is interesting to notice that compound VII is visibly colorless (λ_{max} 318 mμ), whereas XI appears yellow to the eye (λ_{max} 362 mμ). This difference is due to the presence of an extra conjugated carboxyl group in XI.

In an effort to obtain other compounds related to VII and VIII, the lactones were reduced in turn with lithium aluminum hydride. The products, presumably diols, were not crystalline, nor were dehydration products derived from them.

The synthesis of VII as described above exemplifies an approach to synthesis of benzsuberenes which eventually may prove to be useful in getting other compounds of that kind. The critical step in such syntheses obviously is reduction of chalcones derived from 2-hydroxyaceto compounds to products suitable for cyclization. A study in this direction has been begun. In preliminary work it was found that 2-hydroxyacetophenone is reduced to 2-ethylphenol in 78% yield under the same conditions used in reduction of I and IV. Complete reduction of a carbonyl group adjacent to a benzene ring in a neutral medium (ethyl acetate) is unusual, since an acidic environment ordinarily is required. Apparently chelation of the carbonyl group with a favorably-situated enol or phenol moiety serves to promote reduction as effectively as does formation of a conjugate acid through addition of an extra source of protons, such as acetic acid. The exact mechanism of this phenomenon is still obscure, but data from experiments now in progress may shed light upon the matter.[7]

Experimental[8]

3-Ethyl-4-hydroxy-6-methyl-5,6-dihydro-2-pyrone (II).—A solution of 19.8 g. of dehydroacetic acid in 450 ml. of ethyl acetate containing 6 g. of 10% palladium–charcoal catalyst[9] was shaken under hydrogen (40 lb.) and warmed gradually to 80° during a period of an hour. Absorption of 2.2 moles of hydrogen took place in 0.6 hour, and an additional 1.1 moles was taken up more slowly (0.7 hour), after which time the reaction became very slow. The mixture was allowed to cool to about 60°, and was filtered. The filtrate was evaporated to a small volume. When crystallization was complete (half-hour at room temperature) the product was collected, washed with 10 ml. of ethyl acetate, and air-dried. There was obtained 8.8 g. of colorless crystals, m.p. 146–148°. Reworking of the filtrates in the same way gave 1.6 g. of additional product, m.p. 145–147°, bringing the yield to 10.4 g. (56%). Recrystallization from ethyl acetate gave a pure sample, m.p. 146–148°. The compound gave a weak green ferric chloride test and was readily soluble in dilute sodium hydroxide solution. The infrared spectrum (chf.) had an intense double peak at 5.68 and 5.81 μ. This band was absent in the spectrum of the crystalline compound (Nujol null), indicating strong association in the solid state.

Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.58; H, 7.65.

The 2,4-dinitrophenylhydrazone formed rather slowly and was recrystallized from ethyl acetate as shiny, yellow crystals, m.p. 197–199°.

Anal. Calcd. for $C_{14}H_{16}O_6N_4$: C, 50.00; H, 4.80. Found: C, 50.01; H, 4.92.

Compound II was recovered unchanged (95%) after heating with 15 parts of polyphosphoric acid for an hour.

Hydrolysis of II.—A sample (2 g.) of II was dissolved in 8 ml. of warm methanol. Two drops of phenol red solution was added, and the solution was titrated with 2% sodium hydroxide solution (2 drops in excess). The solution was refluxed for 8 minutes and was distilled until 15 ml. of distillate had been collected (10 minutes). The **2,4-dinitrophenylhydrazone** of **2-hepten-4-one** was prepared from half of the distillate in the usual way. Recrystallization from ethanol provided red crystals, m.p. 141.5–143°.

Anal. Calcd. for $C_{13}H_{16}O_4N_4$: C, 53.42; H, 5.52. Found: C, 53.21; H, 5.60.

To the other half of the distillate was added 0.5 g. of 10% palladium–charcoal and 100 ml. of ethyl acetate. The mixture was hydrogenated (40 lb.) at 25° for an hour, and the product was isolated as usual.

The 2,4-dinitrophenylhydrazone of di-*n*-propyl ketone was prepared from the crude product. Recrystallization from methanol gave yellow flakes, m.p. 69–70°. The mixed m.p. with an authentic sample of this compound (m.p. 70–71°) was 69.5–70.5°, and the infrared spectra (chf.) of the two samples were identical. The compound depressed the m.p. of the 2,4-dinitrophenylhydrazone of methyl *n*-amyl ketone, and the infrared spectra in this case were not identical.

Acidification of the aqueous residue from hydrolysis resulted in release of carbon dioxide. When II was refluxed with excess dilute sodium hydroxide solution a brown polymer was obtained.

3-β-[(3,4-Dimethoxyphenyl)-propionyl]-4-hydroxy-6-methyl-2-pyrone (IV).—A mixture of 27 g. of III,[1] 10 g. of 10% palladium–charcoal[9] and 500 ml. of ethyl acetate was shaken under hydrogen (40 lb.) and warmed gradually (0.5 hour) to 80°. About 1.3 moles of hydrogen was taken up rapidly (0.2 hour), and then the rate of absorption decreased abruptly. The shaking was stopped after an hour, when 1.4 moles of hydrogen had been consumed. The mixture was cooled to 65° and filtered. Evaporation of the solvent and trituration of the crystalline residue with ethyl acetate gave 22.7 g. (83%) of product, m.p. 118–122°. Recrystallization from the same solvent gave colorless crystals, m.p. 130–132°. The compound was soluble in 5% sodium hydroxide solution and gave a bright red color with ferric chloride. The infrared spectrum (chf.) had intense peaks at 5.76–5.81 and 6.08 μ. (The infrared spectrum of dehydroacetic acid has an intense band at 5.75–5.82 μ and an intense peak at 6.09 μ.)

Anal. Calcd. for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.23; H, 5.85.

The 2,4-dinitrophenylhydrazone formed rapidly, and was recrystallized from ethyl acetate as dense, red crystals, m.p. 204.5–206°. The infrared spectrum (chf.) of this derivative had a sharp peak at 3.02 μ, an intense double peak at 5.80 and 5.87 μ, a sharp, moderately-intense peak at 6.07 μ, and an intense peak at 6.17 μ.

Anal. Calcd. for $C_{23}H_{22}O_9N_4$: C, 55.42; H, 4.45. Found: C, 55.45; H, 4.21.

Subsequent experiments were carried out using catalyst recovered from the above experiment, and gave better results, presumably because of somewhat decreased catalyst activity. Thus, reduction of 30.8 g. of III in the presence of 10 g. of catalyst recovered from the first run and 500 ml. of ethyl acetate at 80° resulted in absorption of about 1.1 moles of hydrogen in an hour, after which time absorption ceased entirely. The yield of IV was 26.7 g. (86%).

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(5) *Cf.* E. C. Horning and G. N. Walker, THIS JOURNAL, **75**, 4692 (1953); J. Koo and J. L. Hartwell, *ibid.*, **75**, 1625 (1953); G. N. Walker, Ph.D. Thesis, University of Pennsylvania, Phila., Penna., 1951 (Part 4).

(6) E. C. Horning *et al.*, THIS JOURNAL, **72**, 4840 (1950).

(7) NOTE ADDED IN PROOF.—H. Smith, *J. Chem. Soc.*, 803 (1953), observed that 2-acetylcyclohexan-1,3-dione is hydrogenated mainly to 2-ethylcyclohexan-1,3-dione in ethanol in the presence of alkali which promotes enolization of the acetyl compound, but that in ethanol alone the main product was 2-acetylcyclohexanone. The solvent appears to be critical in reductions of this kind, and in fact the selectivity of the process may depend as much upon such factors as upon steric effects.

(8) Melting points are corrected. I am indebted to Dr. William C. Alford and his staff for microanalytical data, and to Mr. H. Franklin Byers and Miss Catherine Monaghan for spectra.

(9) Obtained from Matheson, Coleman and Bell Co., Inc.

Hydrolysis of IV.—A sample (1.0 g.) of IV was refluxed with 50 ml. of 5% sodium hydroxide solution for an hour. Acidification of the cooled, filtered solution gave gummy crystals. Trituration with ether gave 0.3 g. of colorless crystals, m.p. 96–98°. The mixed m.p. with authentic β-(3,4-dimethoxyphenyl)-propionic acid,[10] m.p. 96–98°, was not depressed, and the infrared spectra (chf.) of the samples were identical.

3-[γ-(3,4-Dimethoxyphenyl)-propyl]-4-hydroxy-6-methyl-5,6-dihydro-2-pyrone (V).—Hydrogenation of 10.2 g. of IV in the presence of 6 g. of fresh 10% palladium–charcoal[9] and 300 ml. of ethyl acetate at 40 lb. and 80° resulted in absorption of 3.2 moles of hydrogen in 0.8 hour, after which time no further uptake was observed. The product was isolated as described in the preceding experiment. When first prepared, this product did not crystallize immediately. It was purified by dissolving it in 5% sodium hydroxide solution and washing the alkaline solution with ether–ethyl acetate (which removed 0.4 g. of neutral material); later the compound was recovered by acidification and extraction with ethyl acetate. The organic solution was dried (magnesium sulfate) and the solvent was evaporated. The material crystallized after standing several days (in later experiments the crude product crystallized immediately when seeded). Trituration with ether–ethyl acetate gave 7.8 g. (80%) of colorless crystals, m.p. 121.5–123°, raised to 125–126° after recrystallization from ethyl acetate. The compound gave a weak green color with ferric chloride. Reaction with 2,4-dinitrophenylhydrazine was slow (2 days) and gave viscous, red oil. The infrared spectrum (chf.) had an intense doublet at 5.69 and 5.81 μ.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.79; H, 7.24.

It was possible to reduce III directly to V, using a larger proportion of catalyst to compound. Thus hydrogenation of 14.4 g. of III in the presence of 9 g. of 10% palladium–charcoal in 500 ml. of ethyl acetate resulted in rapid absorption of 2.2 moles of hydrogen (12 minutes) at 25–40° and then slower absorption (1.5 hours) of 2.3 moles at 80°. The product, isolated and purified as described above, amounted to 8.5 g. (61%).

Methyl 4-(3,4-Dimethoxyphenyl)-butyl Ketone (VI).—A solution of 1.4 g. of V in 100 ml. of 5% sodium hydroxide solution was refluxed 3.5 hours. The cooled mixture was extracted with ether. Carbon dioxide was released from the aqueous solution, upon acidification. The ether solution was washed with 2 portions of water and was dried over magnesium sulfate. Evaporation of the solvent gave 0.8 g. of yellow oil, the infrared spectrum of which (chf.) had a sharp, intense peak at 5.87 μ. **The 2,4-dinitrophenylhydrazone** was recrystallized from ethanol–ethyl acetate; yellow crystals, m.p. 119–120°.

Anal. Calcd. for $C_{20}H_{24}O_6N_4$: C, 57.68; H, 5.81. Found: C, 57.93; H, 5.82.

2,3-Dimethoxy-5-(β-hydroxypropyl)-6-carboxybenzsuber-5-ene Lactone (VII).—A mixture of 8.5 g. of V and 120 g. of polyphosphoric acid was heated to 85° on a steam-cone and stirred for 1.9 hours. A chartreuse suspension was formed at first, and later a deep red solution was obtained. The cooled solution was treated with ice and stirred until hydrolysis was complete. The greenish gum was extracted with ethyl acetate and ether. The organic solution was washed successively with one portion of water, 3 portions of 5% sodium hydroxide solution and 2 more portions of water, and was dried (magnesium sulfate). Evaporation of the solvents gave 2.1 g. of viscous, bright-yellow oil, which soon crystallized partly. The crystals were very sparingly soluble in ether. Trituration with ether and a little ethyl acetate gave 1.0 g. (12.5%) of pale-yellow crystals, m.p. 149–152°. Recrystallization from ethyl acetate afforded colorless crystals, m.p. 154.5–156°. The infrared spectrum (chf.) had an intense peak at 5.88–5.92 μ. The ultraviolet spectrum (ethanol) had λ_{max} 224, 248, 293 and 318 mμ (log ϵ 4.09, 4.11, 3.94 and 4.03, respectively); the most pronounced minimum occurred at 268 mμ (log ϵ 3.61).

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.71; H, 6.97.

Acidification of the sodium hydroxide solutions from the work-up gave viscous, brown oil. The material was extracted with ethyl acetate; the organic solution was washed with water, dried, and evaporated. The material crystallized partly after several days. Trituration with ether–ethyl acetate returned 0.9 g. of unchanged V, m.p. 120–123°. The yield of VII based on V consumed was 14%.

Evaporation of the filtrate from trituration of VII gave 1.0 g. of neutral, orange glass. The infrared spectrum (chf.) of this substance had peaks at 5.83, 5.93 and 6.10 μ. The material gave a dark-red precipitate with 2,4-dinitrophenylhydrazine, but no pure derivatives could be isolated.

Compound VII dissolved in boiling 5% sodium hydroxide solution (10 minutes). Acidification of the solution at ice temperature resulted in nearly quantitative recovery of VII. Similar results were obtained when VII was boiled with 5% sodium hydroxide for an hour, or allowed to stand in sodium methoxide–methanol solution for 3 days. Treatment of VII with hot 20% sodium hydroxide solution resulted in formation of intractable gum.

Reduction of 0.3 g. of VII with 1.3 g. of lithium aluminum hydride in 400 ml. of dry ether afforded 0.3 g. of colorless glass. The infrared spectrum of this material had a strong band at 2.93 μ, a weak band at 2.76 μ, and no carbonyl peak. The substance was treated with 30 ml. of benzene containing 1 drop of benzenesulfonic acid and the solution was refluxed under a constant water-separator for 1 hour. The neutral product (0.16 g.) was a bright-yellow oil, the infrared spectrum of which did not have hydroxyl or carbonyl peaks. Attempts to prepare crystalline derivatives from these products were not successful.

Oxidation of VII with potassium permanganate in 2% sodium hydroxide solution gave an ill-defined mixture of products.

2,3-Dimethoxy-5-(β-hydroxypropyl)-6-carboxybenzsuberan Lactone (VIII).—A solution of 0.4 g. of VII in 150 ml. of ethyl acetate containing 1.2 g. of 10% palladium-charcoal[9] was shaken under hydrogen (40 lb.) at 80° for 2 hours. Filtration of the catalyst and evaporation of the solvent gave 0.4 g. of colorless crystals, m.p. 155–164°. Recrystallization from ethyl acetate and cyclohexane afforded pure material, m.p. 167.5–169.5°. The infrared spectrum (chf.) had a sharp, intense peak at 5.80 μ. The ultraviolet spectrum (ethanol) had λ_{max} 233 and 285 mμ (log ϵ 3.91 and 3.53, respectively).

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.47; H, 7.82.

Reduction of VIII with excess lithium aluminum hydride in ether gave a colorless, glassy product, as with VII. The infrared spectrum (chf.) had peaks at 2.76 and 2.94 μ, and was similar to, but not identical with, the spectrum of the lithium aluminum hydride reduction product from VII. Dehydration of the substance in the presence of acids did not afford a crystalline product.

2,3-Dimethoxy-5-(β-hydroxypropyl)-6-carboxybenzsuberan (IX).—A sample (0.2 g.) of VIII was treated with 10 ml. of 5% sodium hydroxide solution, and the mixture was warmed on a steam-cone for 20 minutes. The crystals dissolved in 7 minutes. The solution was chilled in ice, acidified slowly with hydrochloric acid, and was kept at 0° until crystallization was complete (1 hour). The crystals were collected, washed with a small portion of cold water, air-dried, and recrystallized from ethyl acetate–methanol. There was obtained 0.14 g. of colorless crystals, m.p. 176–178° dec. The compound was soluble in sodium bicarbonate solution. The infrared spectrum (Nujol) had peaks at 2.85 and 5.83 μ. The acid loses water at the melting point and returns to lactone VIII.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.37; H, 7.92.

1,2-Dimethoxy-5,6-dicarboxybenzsuber-5-ene Anhydride (XI). (A) Reformatsky Reaction.—A mixture of 55 g. (0.84 atom) of activated 30-mesh zinc, 34 g. (0.205 mole) of redistilled 2,3-dimethoxybenzaldehyde, 41 g. (0.229 mole) of methyl γ-bromocrotonate and 300 ml. of dry benzene was treated with a trace of iodine and was refluxed and stirred vigorously for 3 hours. The cooled suspension was treated with dilute acetic acid and was diluted with ether. The organic solution was washed with successive portions of 10% hydrochloric acid, 5% sodium hydroxide solution, dilute acetic acid, sodium bicarbonate solution, and water, and was dried over magnesium sulfate. (B) **Dehydration:** The solution was treated with 15 g. of phosphorus oxychloride and was allowed to stand for one hour. The neutral product was isolated as usual. Distillation *in vacuo* gave

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[10] W. H. Perkin and R. Robinson, *J. Chem. Soc.*, 1080 (1907).

10.5 g. (20%) of yellow oil, b.p. 180–200° (3.0 mm.). (C) **Hydrogenation**: The ester from (B) was shaken under hydrogen (40 lb.) at room temperature for 8 hours in the presence of 2 g. of 5% palladium–charcoal and 100 ml. of ethyl acetate. The product was isolated as usual. Distillation *in vacuo* gave 6.2 g. (58%) of oil, b.p. 160–180° (3.0 mm.). This product gave negative tests with permanganate and with bromine. (D) **Glyoxylation**: Reaction of product C with excess ethyl oxalate in the presence of sodium ethoxide in dry ether according to the usual procedure gave 68% of alkali-soluble, red oil, which gave a red-purple ferric chloride test. (E) **Cyclization and Hydrolysis**: A solution of 5.9 g. of enol from (D) in 20 ml. of 85% phosphoric acid was chilled in ice and treated with a cold solution of 25 ml. of concd. sulfuric acid and 25 ml. of 85% phosphoric acid. The solution was kept at ice temperature for 10 days, and was hydrolyzed with ice and water. The gummy product was washed with dilute sodium hydroxide solution, and the remaining neutral material was warmed with 40 ml. of 5% sodium hydroxide solution on a steam-cone for 20 minutes. The mixture was filtered. The alkaline solution was washed with ether and was acidified with hydrochloric acid. Yellow crystals were deposited upon heating the turbid solution, or after standing several days at room temperature. The crystals were washed with water and triturated with ethanol. There was obtained 1.1 g. of anhydride, m.p. 169–172°. Recrystallization from ethyl acetate gave yellow crystals, m.p. 172–174°. The infrared spectrum (chf.) had an intense double peak at 5.48 and 5.68 μ and a moderately strong peak at 6.18 μ.

Anal. Calcd. for $C_{15}H_{14}O_5$: C, 65.68; H, 5.15. Found: C, 65.68; H, 5.28.

The ultraviolet spectrum (ethanol) had λ_{max} 237 and 362 mμ (log ϵ 3.95 and 3.90, respectively) with minima at 227 and 275 mμ (log ϵ 3.91 and 3.45, respectively) and a point of inflection at 308 mμ (log ϵ 3.61). The spectrum of IX in sodium hydroxide solution had λ_{max} 274 mμ (log ϵ 4.11).

2-Ethylphenol.—A mixture of 18.0 g. of *o*-hydroxyacetophenone, 5 g. of 10% palladium–charcoal[9] and 400 ml. of ethyl acetate was shaken under hydrogen (40 lb.) at 80°. About 2.5 moles of hydrogen was consumed in 1.4 hours, after which time the reaction became very slow. Shaking was stopped after 2 hours, and the mixture was filtered. The solvent was evaporated. Distillation of the residue afforded 12.6 g. (78%) of colorless oil, b.p. 204–208°. The material had a strong characteristic odor, was soluble in dilute sodium hydroxide solution, and gave a deep blue ferric chloride test. **2-Ethylphenoxyacetic acid** was prepared, following the usual procedure; colorless crystals, m.p. 138–140° (lit.[11] m.p. 140–141°).

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(11) W. Steinkopf and T. Höpner, *J. prakt. Chem.*, [2] **113**, 140 (1926).

BETHESDA 14, MARYLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE VIRGINIA POLYTECHNIC INSTITUTE]

The Use of Alumina in Aromatic Cyclodehydration[1,2]

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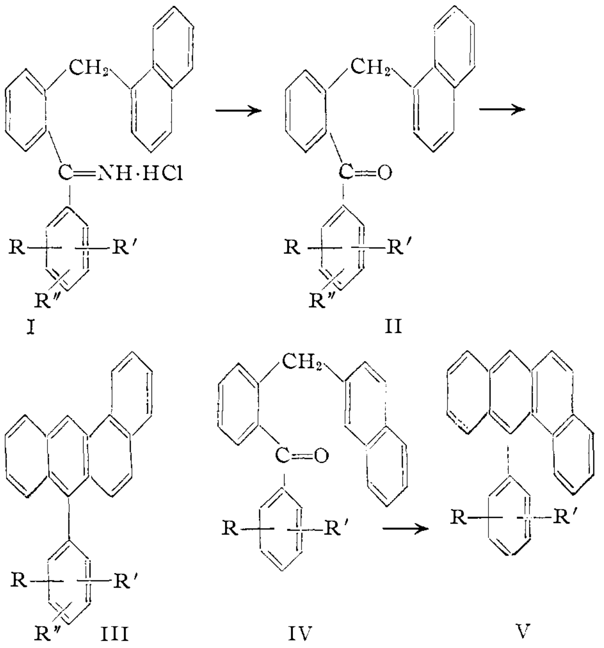
RECEIVED NOVEMBER 21, 1955

A new procedure employing alumina has been successfully applied to the aromatic cyclodehydration of ketones to hydrocarbons.

Although the cyclization of ketones to hydrocarbons has generally proceeded quite well in solution under the influence of heat and acids,[3-7] sterically hindered ketones have failed to cyclize under these conditions.[5,7] So for example 2-(1-naphthylmethyl)-2′,6′-dimethylbenzophenone (II, R,R′ = 2′,6′-dimethyl, R″ = H), 2-(2-naphthylmethyl)-2′,6′-dimethylbenzophenone (IV, R,R′ = 2′,6′-dimethyl) and 2-(1-naphthylmethyl)-2′,4′,6′-trimethylbenzophenone (II, R,R′,R″ = 2′,4′,6′-trimethyl) are cleaved under the usual cyclizing conditions[5] to give 1,2-benzanthracene. This indicated the necessity of devising a new method or at least of changing the conditions of the cyclization. Cold concentrated sulfuric acid led invariably to sulfonated, water-soluble products. Phosphorus pentoxide and 100% phosphoric acid yielded small amounts of green fluorescent oils which could not be crystallized. Finally a successful method was devised which followed a rather unconventional line. The previous cyclizations were carried out in solution with catalysis by a strong mineral acid. The new method consists of heating the ketone with powdered aluminum oxide to 240–280° under reduced pressure. This procedure yielded excellent results in the cases of the hindered ketones (II and IV with



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(1) Presented before the Division of Organic Chemistry at the 128th Meeting of the American Chemical Society, Minneapolis, Minn., Sept., 1955.

(2) This paper has been abstracted from the Doctorate thesis presented to the Virginia Polytechnic Institute by Alexej Bořkovec in 1955.

(3) C. K. Bradsher, THIS JOURNAL, **62**, 486 (1940).

(4) F. A. Vingiello, A. Bořkovec and J. Shulman, *ibid.*, **77**, 2320 (1955).

(5) F. A. Vingiello and A. Bořkovec, *ibid.*, **77**, 3413 (1955).

(6) F. A. Vingiello and A. Bořkovec, *ibid.*, **77**, 4823 (1955).

(7) Presented before the Section of Organic Chemistry at the Seventh Southeastern Regional Meeting of the American Chemical Society, Columbia, South Carolina, Nov., 1955.