[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Macro Rings. X. A New Reaction for the Conversion of Acyloins to Ketones

BY DONALD J. CRAM AND MARTIN CORDON

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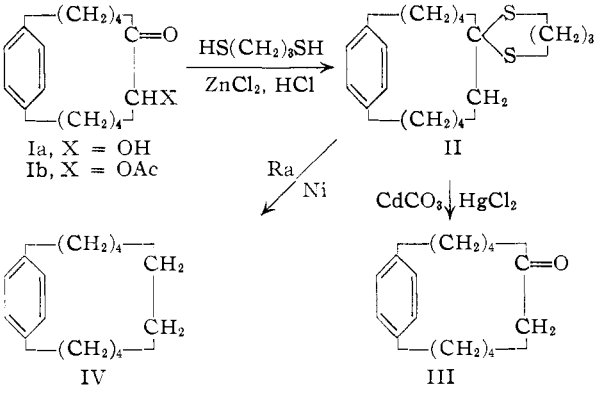
Treatment of a number of acyloins and acyloin acetates with 1,3-propanedithiol, hydrogen chloride and zinc chloride in benzene provided in each case a simple mercaptal, the hydroxyl or acetoxyl groups having been replaced with hydrogen. Ketones subsequently were obtained by ordinary hydrolytic methods.

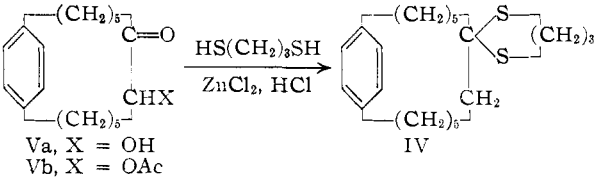
Although a number of methods have been devised for converting acyloins to ketones employing zinc and acid,[1] in our hands the ketonic product always has been obtained in yields inferior to those of the saturated hydrocarbon arising by the Clemmensen reduction of the ketone.[2] Recently a convenient method for the removal of the carbonyl function from an acyloin has been described.[2c,3] The acyloin acetate is converted to a mercaptal which is then reduced with nickel to provide the simple acetate. In attempting to apply this method to a number of cyclic acyloins, we encountered a new reaction which provides a route for the conversion of acyloin to ketone or to hydrocarbon.

Treatment of either acyloin Ia or acyloin acetate Ib with 1,3-propanedithiol, zinc chloride and dry hydrogen chloride in benzene provided the mercaptal II (75 and 83% yields, respectively), in which the hydroxyl or acetoxyl of the starting material

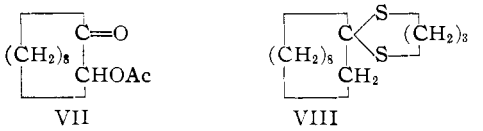


was replaced with hydrogen. This substance was identified by its hydrolysis[4] to ketone III (85% yield) which has been reported previously,[2a] and by its reduction with nickel to the known saturated hydrocarbon.[2a] The ultraviolet absorption spectrum of this mercaptal (II) possessed a band at λ_{max} 248 mμ (log ϵ 3.04) which is undoubtedly due to the mercaptal linkage. The fact that this band is shifted from λ_{max} 235–240 mμ which is characteristic of open chain mercaptals[5] is probably a consequence of the mercaptal linkage being incorporated in a six-membered ring.

That the reaction is not peculiar to this particular system was demonstrated by converting acyloin Va and acyloin acetate Vb to mercaptal VI (λ_{max} 249 mμ, log ϵ 2.91), sebacoin acetate (VII) to mercaptal VIII (λ_{max} 248 mμ, log ϵ 2.86), and



acetoin to its corresponding mercaptal (λ_{max} 249 mμ, log ϵ 2.91). The relatively low yields (34 and 16%, respectively) of mercaptal in the last two cases probably was due to their liquid character which made them difficult to isolate in a pure state on the scale employed.



Although obvious applications of the reaction to steroids and carbohydrates might be possible, these were not investigated.

Attempts to carry out the reaction employing ethyl mercaptan and Ia failed, as did the reaction utilizing Ia and 1,3-propanedithiol without the zinc chloride catalyst.

A number of reductions involving mercaptans as reducing agents have been reported. Thus azomethine linkages have been reduced[6] as have certain ketones.[7] In an attempt to uncover a clue with respect to the mechanism of the acyloin reduction,[8] the fate of the reducing agent was investigated. From the mixture of materials produced in these reactions was isolated a material whose properties corresponded to those reported for trimethylene disulfide dimer.[9,10] This fact suggests

(1) (a) V. Prelog, K. Schenker and H. H. Gunthard, *Helv. Chim. Acta*, **35**, 1598 (1952); (b) Firmenich and Co., British Patent 663,183 (1951), or *C. A.*, **47**, 608 (1953); (c) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

(2) (a) D. J. Cram and H. U. Daeniker, *ibid.*, **76**, 2743 (1954); (b) J. Abell and D. J. Cram, *ibid.*, **76**, 4406 (1954); (c) J. F. Sheehan, R. A. Coderre and P. A. Cruickshank, *ibid.*, **75**, 6231 (1953); (d) H. C. Brown and M. Borkowski, *ibid.*, **74**, 1901 (1952).

(3) (a) M. Levitz, *ibid.*, **75**, 5352 (1953); (b) M. N. Huffman and M. H. Lott, *ibid.*, **71**, 719 (1949).

(4) M. L. Wolfrom, *ibid.*, **51**, 2188 (1929).

(5) E. A. Fehnel and M. Carmack, *ibid.*, **71**, 84 (1949).

(6) H. Gilman, J. L. Towle and R. K. Ingham, *ibid.*, **76**, 2920 (1954).

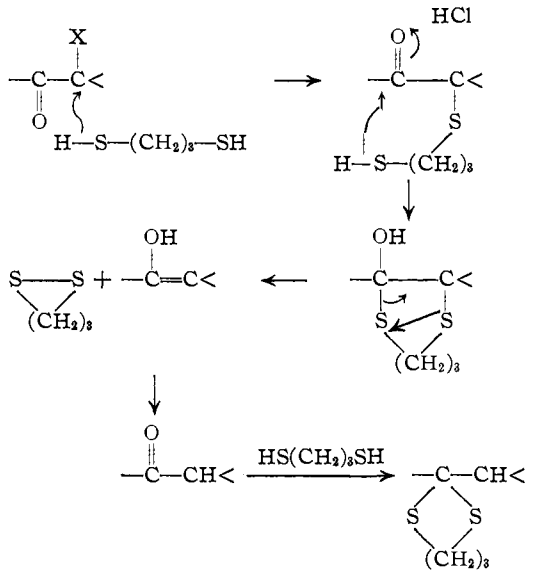
(7) H. Hauptmann, *ibid.*, **69**, 562 (1947).

(8) For another example of an abnormal reaction of an acyloin with a mercaptan, see E. Campaigne and J. R. Leal, *ibid.*, **76**, 1272 (1954).

(9) (a) W. Autenrieth and K. Wolff, *Ber.*, **32**, 1370 (1899); (b) Yu. K. Yur'ev and I. S. Levi, *Doklady Akad. Nauk S.S.S.R.*, **73**, 953 (1950), or *C. A.*, **45**, 2934 (1951).

(10) J. A. Barltrop, P. M. Hayes and M. Calvin [THIS JOURNAL, **76**, 4348 (1954)] have reported that trimethylene disulfide itself is an oil whose formation from 1,3-propanedithiol is accompanied by the formation of its dimer. Since the monomer readily undergoes polymerization under a variety of circumstances to give materials similar to those observed in the present investigation, it is possible that trimethylene disulfide is a precursor of some of these substances. A second possible source of the disulfide is the unused 1,3-propanedithiol which is oxidized by air to give disulfide.

that the mechanism for the reaction might involve a sequence similar to that formulated.



Experimental

Reaction of 1,3-Propanedithiol with 5-Acetoxy-6-keto-[10]paracyclophane (Ib).[11]—The reagent 1,3-propanedithiol was prepared in 41% yield,[12] b.p. 70–72° (18 mm.), $n^{25}D$ 1.5375. Acetate Ib[2a] (1.00 g.), 1.6 ml. of the dithiol and 1.5 g. of powdered freshly fused zinc chloride were stirred in 30 ml. of dry benzene. The mixture was saturated with dry hydrogen chloride until a dark red oil separated. The mixture was stirred at room temperature for two hours and the solution was decanted from the second phase. The solution was washed with dilute base and water, dried and evaporated under reduced pressure. The residual yellow oil was crystallized from 30 ml. of 95% ethanol, 1st crop, 0.70 g., m.p. 87–89°; 2nd crop, 0.10 g., m.p. 86.5–88.5 (yield 83%). A recrystallization of the material provided an analytical sample, m.p. 88–89.5°, of mercaptal II.

Anal. Calcd. for $C_{19}H_{28}S_2$: C, 71.18; H, 8.80. Found: C, 71.36; H, 8.91.

The above procedure was repeated with 1.07 g. of 5-hydroxy-6-keto-[10]-paracyclophane (Ia), 1.00 g. (75%) of mercaptal II being isolated, m.p. 87–89°.

Reaction of 1,3-Propanedithiol with 6-Acetoxy-7-keto-[12]paracyclophane (Vb).—Acetate Vb was prepared from the corresponding acyloin[13] by the usual acetic anhydride–pyridine method in 75% yield, colorless oil (Vb), distilled at a pot temperature of 170° (0.5 mm.); $n^{25}D$ 1.5190.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.92; H, 8.91. Found: C, 76.12; H, 9.20.

Application of the procedure employed for the preparation of II from Ib to this acetate (0.800 g.) gave 0.600 g. (72%) of mercaptal VI, m.p. 55–58° (colorless plates) from 95% ethanol. Two recrystallizations of the material from methanol gave m.p. 56–59°.

Anal. Calcd. for $C_{21}H_{32}S_2$: C, 72.35; H, 9.27. Found: C, 72.41; H, 9.36.

When acyloin Va was employed (0.500 g.), mercaptal VI was obtained in 56% yield, m.p. 56.5–58°.

Reaction of 1,3-Propanedithiol with Sebacoin Acetate.—Sebacoin acetate ($n^{25}D$ 1.4757),[14] 2.00 g., was allowed to react with 2 ml. of 1,3-propanedithiol, 4 g. of powdered freshly fused zinc chloride in 30 ml. of benzene and dry hydrogen chloride. The oil isolated from this reaction was purified by chromatography on neutral alumina followed by distillation (pot temperature of 160° at 0.8 mm.) to give 0.77 g. (34%) of colorless oil (VIII), $n^{25}D$ 1.5640.

Anal. Calcd. for $C_{13}H_{24}S_2$: C, 63.87; H, 9.92. Found: C, 64.15; H, 9.72.

Reaction of 1,3-Propanedithiol with Acetoin.—The above procedure was applied to 1.33 g. of acetoin and 2.5 ml. of the mercaptan. The residual oil and solid obtained by evaporation of the benzene was dissolved in a small amount of methanol. Water was added to the resulting solution, and the oil that separated was extracted with ether. The ether solution was dried, evaporated and the residual oil distilled at a pot temperature of 110° (7 mm.) to give 0.405 g. of colorless oil mercaptal of 2-butanone, $n^{25}D$ 1.5415.

Anal. Calcd. for $C_7H_{14}S_2$: C, 51.80; H, 8.69. Found: C, 51.26; H, 8.69.

Isolation of Trimethylenedisulfide Dimer.—When the benzene was removed in the above procedures, a white amorphous material remained which was insoluble in most organic solvents, and only slightly soluble in hot benzene or chloroform. Thus the mercaptal was separated by its solution in hot alcohol. The residual material in the preparation of II from Ia was recrystallized from pyridine to give 0.80 g. of trimethylene disulfide dimer, m.p. 76–77.5° (literature,[9a] m.p. 76.5–77.5°). This material was sublimed at 100° and 0.5 mm., m.p. 77–79°.

Anal. Calcd. for $C_3H_6S_2$: C, 33.93; H, 5.70. Found: C, 34.12; H, 5.93.

Hydrolysis of Mercaptal II to 5-Keto[10]paracyclophane (III).—A mixture of 2.08 g. of the thioketal, 8 g. of mercuric chloride, 60 ml. of acetone, 8 g. of cadmium carbonate and 10 ml. of water was stirred for 22 hours. Additional quantities of cadmium carbonate were added occasionally. The acetone solution was then filtered, and the solvent was evaporated under reduced pressure. The residual oil was extracted with pentane, the pentane solution was washed with water, potassium iodide solution and water. The solution was dried, the solvent evaporated, and the oil that remained was distilled at a pot temperature of 150–160° (0.5 mm.) to yield 1.31 g. (85%) of colorless oil (III), $n^{25}D$ 1.5385. A sample of this material was converted to its 2,4-dinitrophenylhydrazone in 80% yield, m.p. 134–136°, undepressed by admixture with authentic derivative of 5-keto-[10]paracyclophane (ketone C, previously described, $n^{25}D$ 1.5383[2a]).

Hydrogenolysis of Mercaptal II.—The mercaptal (0.96 g.) was refluxed for 24 hours with 10 g. of Raney nickel (W-1) in 100 ml. of absolute ethanol. The nickel was collected and washed with ethanol, and the solvent was then removed under reduced pressure. The oil that remained was distilled at a pot temperature of 110–120° at 0.5 mm. to yield 0.45 g. of colorless oil of [10]paracyclophane (IV).[2a] The oil was redistilled from sodium for analysis ($n^{25}D$ 1.5220).

Anal. Calcd. for $C_{16}H_{24}$: C, 88.82; H, 11.12. Found: C, 88.69; H, 11.41.

LOS ANGELES, CALIFORNIA

(11) For system of nomenclature, see D. J. Cram and J. Abell, THIS JOURNAL, **77**, 1179 (1955).

(12) (a) J. R. Meadow and E. E. Reid, *ibid.*, **56**, 2177 (1934); (b) S. D. Simpson, *Can. J. Research*, **25B**, 20 (1947).

(13) D. J. Cram, N. L. Allinger and H. Steinberg, THIS JOURNAL, **76**, 6132 (1954).

(14) A. T. Blomquist, R. E. Burge, Jr., and A. C. Sucsy, *ibid.*, **74**, 3636 (1952).