An Improved Procedure for the Direct Oxidation of Olefins to α-Diketones by Potassium Permanganate in Acetic Anhydride

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Oxidation of symmetrical disubstituted olefins with potassium permanganate in cold acetic anhydride provides ready access to the rather rare α-diketone functional group.[2] In the published[2] procedure, the reaction mixture is worked up by first adding cold 1:1 ethyl acetate–hexane and then ice-cold aqueous sodium bisulfite. After this extraction the final steps involve washing the water, removal of anhydrides, and product purification.

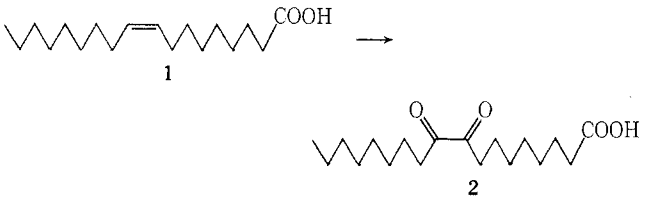
In larger scale reactions (>500 ml of acetic anhydride) the work-up was sometimes unpredictably violent and exciting. In particular, if the ethyl acetate–hexane extracting solvent and the aqueous bisulfite solution were not adequately cooled, and if the separation were not completed quickly enough, vigorous hydrolysis of the acetic anhydride would commence. This exothermic reaction caused the organic solvents to boil out of the separatory funnel. We now report an improved larger scale extraction procedure which significantly reduces the possibility of these runaway hydrolyses.

We have found that addition of sodium chloride to the aqueous bisulfite permits the aqueous extracting solvent to be cooled below 0°, helps keep water out of the organic phase, and gives a much more rapid phase separation. The first aqueous extract can thus be quickly removed before hydrolysis of the acetic anhydride has a chance to get started.

We have also used somewhat less acetic anhydride than would be calculated by a direct scale up of the earlier procedures.[2] This simplifies the work-up but the more concentrated conditions require mechanical rather than magnetic stirring, since the reaction mixture becomes very viscous after the permanganate has been added.

This improved procedure does not significantly increase the yield;[3] it does, however, increase the safety and convenience of the reaction (Scheme I).

Scheme I



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Experimental Section

Technical oleic acid (111 g, 0.3 mol)[4] was stirred mechanically overnight with 1 l. of acetic anhydride[5] under nitrogen.[6] The resulting clear solution was cooled to −5° in a large ice-salt bath, and then 251 g (1.59 mol) of potassium permanganage[7] was slowly added over a 1-hr period keeping the pot temperature <5°. Stirring in the ice-salt bath was continued for another 90 min (during which time the pot temperature rose to a maximum of 10°). Then 1.5 l. of 2:1 ethyl acetate–hexane was cooled to −10° and added to the reaction vessel. A chilled (<−5°) aqueous extracting solution had previously been prepared by mixing 100 g of $NaHSO_3$, 0.5 l. of water, and 0.5 l. of saturated NaCl solution, cooling in an ice-salt bath, and then adding ice directly to this solution for the final cooling.[8] The cold aqueous solvent was added to the reaction vessel. After a few minutes of stirring, the resulting dark liquid was poured into a 6-l. separatory funnel. The aqueous phase was drawn off as soon as it separated. The organic phase was usually still purple; if so, it was washed again with cold aqueous $NaHSO_3$–NaCl, whereupon it became yellow. Finally, the organic phase was washed several times with water and then most of the solvent and acetic anhydride were removed on a rotary evaporator at 100°.[9]

The resulting oil was dissolved in 250 ml of pyridine, and 125 ml of water was slowly added with stirring in an ice bath. The solution was stirred at room temperature overnight to hydrolyze any remaining acid anhydrides. Ether (2 l.) was added and the pyridine was removed by washing the organic phase with aqueous HCl until the aqueous extract remained acidic. The resulting yellow ether solution was taken to dryness at 50° on a rotary evaporator. The yellow solid was recrystallized from 1 l. of 95% ethanol to give 43.6 g (0.14 mol) of 9,10-diketostearic acid (**2**, 46% isolated yield[3]): mp 85.0–85.5°; uv max (95% C_2H_5OH) 270 mμ (log ε 1.665) and 425 (1.26) [lit.[11] mp 85–86°, uv max 270 mμ (log ε 1.7)]; ir (KBr disk) 3100 (OH), 2910, 2850, and 1720–1700 cm^{-1} (s, C=O); nmr ($CDCl_3$) δ 7.34 (s, 1, -COOH), 2.73 (t, 4, J = 7 Hz, CH_2COCO), 2.25 (t, 2, J = 6 Hz, CH_2COOH), 1.32 (m, 22, CH_2), and 0.90 ppm (3, CH_3).

Anal. Calcd for $C_{18}H_{32}O_4$: C, 69.19; H, 10.32. Found: C, 69.19; H, 10.63.

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References and Notes

(1) (a) National Science Foundation Predoctoral Fellow, 1970–1973; Goodyear Fellow, 1973–1974. (b) Camille and Henry Dreyfus Teacher-Scholar grant recipient; Alfred P. Sloan Fellow, 1973–1975.

(2) K. B. Sharpless, R. F. Lauer, O. Repič, A. Y. Teranishi, and D. R. Williams, *J. Amer. Chem. Soc.*, **93**, 3303 (1971).

(3) Since the original oleic acid was 75% pure, the overall yield of α-diketone was 46%, isolated. This represents a slight improvement over our earlier (ref 2) result of a 42% yield by glc. The potassium permanganate–acetic anhydride oxidation usually gives lower yields with cis, as opposed to trans, olefins (ref 2).

(4) Technical oleic acid (75%) was used; this amount contains 83 g of oleic acid. Since the diketone product can be obtained in high purity from this inexpensive-grade starting material, use of more expensive, higher purity oleic acid seems unnecessary.

(5) Eastman Kodak 99+% acetic anhydride was used as received.

(6) Initially, the oleic acid does not dissolve in acetic anhydride; however, after stirring overnight a homogeneous solution is obtained. Presumably, the oleic–acetic mixed anhydride is more soluble.

(7) Fisher reagent-grade permanganate was pulverized with a mortar and pestle prior to addition.

(8) Some of the $NaHSO_3$ may not dissolve. Should this occur, any undissolved solid is simply run out of the bottom of the separatory funnel along with the aqueous phase.

(9) This high-temperature removal of solvent should acetylate any α-hydroxy ketones present. The less crystalline α-acetoxy ketones are more soluble, and thus stay in solution during the ethanol recrystallization, eliminating the problem of α-hydroxy ketone impurities in the product. If desired, the α-acetoxy ketones can be hydrolyzed and then oxidized by cupric acetate to more α-diketone (ref 2).[10] However, because of the low cost of oleic acid, the cupric acetate procedure was not used to increase the overall yield in this oxidation. Not all α-diketones would survive this high-temperature step; for more sensitive compounds, ref 2 describes gentler procedures which may be used for final isolation after the initial extraction is completed.

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