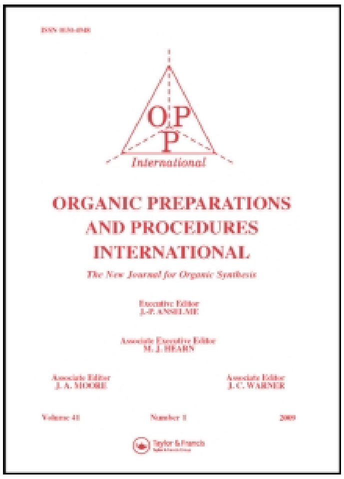

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PREPARATION OF *trans*-2-OCTADECENOIC ACID

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PREPARATION OF trans-2-OCTADECENOIC ACID[1]

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trans-2-Octadecenoic acid (I), the C_{18} member of a series of homologs of considerable interest as intermediates in the metabolic oxidation of fatty acids, is available by treatment of α-bromostearic acid with KI, followed by KOH in boiling ethanol, without isolation of the α-iodo intermediate.[2] Although this approach appears attractively simple, the reaction yields α-hydroxy- and -ethoxy substituted products in amounts comparable with that of the desired substance (in addition to others in smaller quantity), which has therefore been difficult to isolate in high purity or in quantity approaching that actually present in the mixture. Gas-chromatographic analysis of the complex reaction mixture and consideration of the physical properties of its various components has permitted design of an isolation procedure that is considerably more effective than those employed by others.[3,4]

EXPERIMENTAL

Myers' directions[3] were followed closely; 14.6 g (0.04 mole) of α-bromostearic acid (recrystallized from acetone at -20° and containing less than 1 mole % stearic acid)[5] was treated first with KI, then with KOH in boiling 95% ethanol[6] to give 11.7 g of water-insoluble acidic products shown by silicic acid column chromatography and glc to contain 6.31 g of I (56% yield), 2.16 g of ethoxystearic acid, 1.94 g of hydroxystearic acid, and about 0.1 g each of stearic, cis-2- and trans-3-octadecenoic acids.[7]

Recrystallization of 11.2 g of this mixture of acids from 40 ml of ether at 4° gave 5.3 g of material containing 76% I, 22% hydroxy- and only 2% ethoxystearic acid. Treatment of this material, dissolved in 10% methanol-ether[8], with ethereal diazomethane gave 5.47 g of mixed methyl esters, which were taken up in 50 ml of n-pentane (0.20 g of insoluble hydroxystearate was allowed to settle out). Four 10-ml aliquots of this solution (1.054 g solute per aliquot) were chromatographed on silicic acid (90 x 33 mm column of 49 g J. T. Baker Chemical Co. "Silicic acid, powder", void volume 50 ml, activated *in situ* by prewashing successively with 100 ml each of acetone, diethyl ether and n-pentane). Successive fractions were eluted first with 100 ml each of pentane and 1% (by vol.) of ether in pentane (the small amounts of *cis*-2-enoate present in the mixture tend to be concentrated in this fraction of material less strongly adsorbed than the desired *trans* isomer) then with 100 ml of 2% ether in pentane and 50 ml of 3% ether in pentane (eluting *trans*-2-enoate) followed with another 50 ml of 3% and 100 ml each of 4 and 5% ether in pentane (residual ethyoxystearate) and finally with 200 ml of ether (hydroxystearate). The column was then reactivated by passage of 100 ml of pentane prior to introduction of the next aliquot of ester solution. Pooled fractions from all four aliquots contained (in order of elution) 99 mg of semisolid material; 3.23 g of methyl *trans*-2-enoate (white solid); 93 mg of yellow oil (ethoxystearate); and 0.72 g of hydroxystearate (solid).

Saponification of methyl *trans*-2-octadecenoate, even under mild conditions (refluxing a solution of 3.23 g of the ester in 38 ml N/2 KOH in 95% ethanol for 1 hr), results in formation of considerable quantities of *trans*-3-octadecenoic (14%) and β-ethoxystearic (10%) acids in addition to the desired product (I).[9] Fortunately, the desired product (I) is the sole component of high crystallizing power in this mixture; crystallization of the crude saponification product (from 3.23 g of ester) from 16 ml of hexane at 4° gives 2.10 g of I (91% of total product in the mixture), as colorless monoclinic prisms, mp. 57.9-58.5°, lit.[3] mp. 58.5°; λ_{max} 210 nm (ϵ 1.36 x 10^4) in isooctane, in good agreement with characteristics of comparable substances.[9,10] This material was shown by glc analysis (as methyl esters) to contain 0.8% stearic and 1.0% 3-octadecenoic acids.

Treatment of I with diazomethane yields methyl *trans*-2-octadecenoate, mp. 33.5-34.5°, lit.[4] mp. 34.5-35°; UV (isooctane) λ_{max} 205 nm (ϵ 1.44 x 10^4)[11]; IR (CCl_4) in good agreement with that reported by Sinclair *et al.*, (mull)[12]: λ_{max} 5.82 μ (C=O stretch), 6.04 (C=C stretch) and 10.21 ("*trans* peak").

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1. This paper is based on work performed under Contract AT(04-1)-GEN-12 between the Atomic Energy Commission and the University of California, Los Angeles.

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3. G. S. Myers, J. Am. Chem. Soc., **73**, 2100 (1951).

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5. α-Bromination of stearic acid is not easily carried to completion; care should be taken that the product contain little starting material lest an additional component — one probably particularly difficult to eliminate — be added to the already complex mixture.

6. Myers[3] does not disclose whether the "alcohol" he employed was 95% or absolute; in our hands use of 95% ethanol yielded material containing more of the desired elimination product.

7. Relative to methyl stearate (r.t.=1), the retention times of these substances in glc (as methyl esters run on a 40 x 0.25 in column of polyethylene glycol succinate supported on Gas-Chrom, obtained from Applied Science Labs., Inc., State College, Pa.) is *c*-2, 1.06; *t*-3, 1.25; *t*-2 (I), 1.70; and EtO, 1.98. Again relative to methyl stearate, the specific responses (tritium-argon detector) of the methyl esters of I and of ethoxystearate are 0.892 and 1.18, respectively.

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9. Cason *et al.* [J. Org. Chem., **18**, 850 (1953)] recognized that the extensive isomerization noted also by them in saponification of analogous α, β-unsaturated esters could be reconciled with the resistance of the corresponding acids to such change reported by Linstead [J. Chem. Soc.,

2579 (1927)] (note also the very minor amount of 3-enoic acid obtained here by action of KOH on α-bromostearic acid) by assuming that the esters suffer prototropic rearrangement prior to saponification; the Δ^2:Δ^3 ratio obtained here (5.2:1) approaches but does not attain the 2.85:1 equilibrium ratio cited by Goldberg and Linstead [J. Chem. Soc., 2343 (1928)] as characteristic of such substances. It seems reasonable to conclude that attack by EtO$^-$ (or by HO$^-$, giving the β-substituted saturated derivatives) as well as deprotonation would be more facile with the neutral esters than with the negatively charged free acid anions.

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11. The ester will react further with excess diazomethane to yield a pyrazoline whose presence is revealed by appearance of additional UV absorption, λ_{max} 278 nm (isooctane), and by evidence of presence of material of greater retention time (in glc) presumably arising by pyrolytic loss of nitrogen.

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