Facile Dehydrobromination of *vic*-Dibromo Fatty Acids: A One-Vessel Bromination-Dehydrobromination[1] of Oleic Acid to Stearolic Acid

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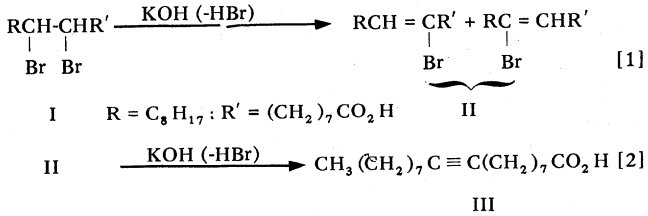
ABSTRACT

The effects of time and temperature on the dehydrobromination by alcoholic KOH of 9,10-dibromostearic acid to 9(10)-bromo-9-octadecenoic and stearolic acid (9-octadecynoic acid) have been studied. Dimethylsulfoxide (DMSO) in n-propanol-KOH solution has been found to be an effective cosolvent-catalyst. In the absence of DMSO, the first monodehydrobromination step to the ethenylene bromide is quantitative in 5 min at 60 C and the second dehydrobromination step to the acetylenic acid is complete in about 6 hr at 100 C. In the presence of DMSO, the dehydrobromination to stearolic acid is quantitative at 100 C in 1-2 hr. A 1-vessel oleic acid bromination-dehydrobromination has been devised to give stearolic acid in 98% yield and purity.

INTRODUCTION

Dehydrohalogenation of *vic*-dihalides in basic media (1,2) has been a common method of preparing acetylenes and functionalized acetylenes. Long-chain acetylenic acids, generally represented by stearolic (9-octadecynoic) acid, have been prepared by dehydrobromination of the dibromo acids in alcoholic base solution in accordance with the Organic Synthesis procedure (3) but yields were low (ca. 30-40%) and reaction times long (8-12 hr). The acetylenic acids were subsequently prepared in improved yields (ca. 50-60%) with sodamide in liquid ammonia (4-7). The disadvantages of this reagent and solvent, namely, the low solubility of fatty acid salts, the pyrophoric hazards of sodium metal and sodamide, inconvenience and toxicity of liquid ammonia and relatively low yields of product preclude their adoption for large-scale preparations.

An alternative approach was devised by Butterfield and Dutton (8), who obtained stearolic acid in 80% yield by dehydrohalogenation in boiling 30% KOH-ethylene glycol solution or in boiling 30% KOH-water solution under pressure at 180 C. The initial dehydrohalogenation step to ethenylene bromides [1] was reported to occur at 160 C with completion to stearolic acid [2] in ca. 4 hr. in the glycol medium and in 5 hr at that temperature in the pressure reaction. This method was offered as a possible industrial procedure but its usefulness is limited by the high temperatures and subsequent extractive steps.



A review of the literature on alkaline dehydrohalogenations showed that the alcoholic base approach has been inadequately studied for details of formation of the intermediate ethenylene halide and acetylenic products. Catalysis in alcoholic base could enhance the reaction rate at lower temperatures and this would provide a safe, convenient and potentially economical method. Since dipolar aprotic solvents have long been known to affect the rate and course of chemical reactions (9-11), dimethylsulfoxide (DMSO) was examined for its effect on this reaction. Although DMSO or dimethylformamide had been used previously in the partial dehydrobromination of methyl dibromostearate with metal cyanates (12), the reaction failed to give methyl stearolate. DMSO was also used recently with potassium-*t*-butoxide as base in the acetylenic functionalization of jojoba oil (13), but this reaction provided no improvement over other methods and gave a product contaminated with isomeric allenic acid. We were indeed able to improve the alcoholic base dehydrohalogenation of 9,10-dibromostearic acid for the quantitative preparation of stearolic acid simply by incorporating DMSO as a cosolvent-catalyst.

The improved synthetic procedure presented in this paper emerged from the determination of the effects of temperature, time and DMSO concentration. On the basis of these data, a simple, rapid 1-vessel procedure for the direct preparation of acetylenic acids from olefinic acids has been devised.

EXPERIMENTAL

Representative Parameter Study

Time studies at 25 C and 60 C in methanol solution and at 100 C in n-propanol solution in the presence or absence of DMSO were performed. A representative experiment with DMSO catalyst is illustrated for a 0.2 M solution of 9,10-dibromostearic acid (DBSA) at 100 C.

A solution of DBSA (4.42 g; 0.01 m) in n-propanol (10 mL) was added to a refluxing solution of n-propanol (35 mL) and potassium hydroxide (3.4 g; 0.06 m) followed by addition of DMSO (4.5 mL; 0.05 m). Samples (2-5 mL) periodically removed for analysis were acidified in cold 5 N hydrochloric acid (25 mL). The oil was extracted with ethyl ether (25 mL), washed with water, dried with a few crystals of sodium sulfate and the ether was evaporated. Methyl esters for gas liquid chromatographic (GLC) analysis were prepared with diazomethane (14).

Preparation of 9,10-Dibromostearic Acid

Bromine (19.3 g, 0.12 m) was added drop by drop to a stirred solution of oleic acid (28.3 g, 0.1 m) in ethyl ether (140 mL) while the temperature was maintained below -10 C. After completion of addition (15 min), the solution was warmed to room temperature (RT), while being stirred for an additional 30 min. Excess bromine was reduced by sodium thiosulfate in the presence of acid. The solution was washed with water, dried and concentrated by evaporation. Yield was 29.5 g (99%; 98% pure dibromide by GLC).

One-Vessel Bromination-Dehydrobromination

A solution of oleic acid (14.1 g; 0.05 m) in ethyl ether (80 mL) was cooled to -10 C in a dry-ice bath. Bromine (9.6 g, 0.06 m) was added drop by drop (15 min for addition) while the temperature was maintained below -5 C. The solution was stirred an additional 15 min in the course of warming to RT and the excess bromine removed by reaction with 2-methyl-2-butene as scavenger. n-Propanol (200

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mL) and KOH (20 gm, 0.36 m) were added and the ether and pentacarbon unsaturated compounds from the scavenger were distilled off. At 60 C, DMSO (18 mL, 0.25 m) was added and the solution refluxed at 100 C for 1 hr. The mixture was cooled to RT, poured into ice-cold 2 N HCl (250 mL) containing ice chips, filtered and washed in the cold mixture. After drying, the yield of stearolic acid was 13.9 g (98%; 98% purity by GLC).

Gas Chromatography (GC)

GLC analysis was performed on a Hewlett-Packard Gas Chromatograph #5830 A. Chromatograms were run on a SCOT capillary column, 50′ × 0.020″, DEGS coated, temperature programmed to 170-190 C flame ionization detector. The injection port was fitted with a glass sleeve to prevent metal-induced decomposition of the halides.

RESULTS AND DISCUSSION

Reactions in refluxing methanol and n-propanol solutions conveniently provided moderate controlled reaction temperatures of 60 C and 100 C, respectively. In the absence of DMSO, the first stage dehydrobromination of dibromo acid to the ethenylene bromo derivative [9(10)-bromo-9 octadecenoic acid] was quantitative in 5 hr at RT and in 5 min at 60 C (Table I). Continued heating for 1 hr at 60 C produced only 2% stearolic acid which indicated low reactivity of the ethenylene bromides to the second HBr abstraction reaction. However, the latter reaction proceeded at 100 C with nearly complete conversion to stearolic acid in 5 hr. The 2-stage reaction in basic propanol is evidently more rapid than that expressed by the extreme conditions of high temperature (3,8) and pressure (8) imposed by earlier investigators.

The addition of DMSO accelerated both dehydrohalogenation steps at rates depending upon the DMSO concentration. In the presence of 20 mol ratio of DMSO/DBSA (dibromostearic acid), the RT dehydrobromination to ethenylene bromide was completed in 15 min compared with 5 hr in the absence of DMSO. The second dehydrobromination leading to quantitative formation of stearolic acid was attained in this DMSO solution in 1.5 hr at 60 C and in 15 min at 100 C. Unfortunately, the advantage of high acceleration at high DMSO concentration is partly offset by the partial solubility of the product in aqueous DMSO. At lower DMSO concentrations, the dehydrobromination is catalyzed by with longer reaction times. Nevertheless, the conditions of 3-5 mol ratio of DMSO/DBSA and 100 C favorably converted the dibromide to stearolic acid within 2 hr, as shown in Table 1. The product was easily isolated by precipitation in acidulated water.

Acetylenes are isomerized to allenes and alternate positions by strong bases, particularly at elevated temperatures. Shani (13) obtained 5-6% allene in dehydrobromination of brominated jojoba oil in DMSO-*t*-BuOK heated at 100 C for 5 hr. The stearolic acid prepared in the present procedure is free of the allene as evidenced in nuclear magnetic resonance (NMR) by the absence of the proton resonance in -C<u>H</u>=C=C<u>H</u>- (2H, q, 4.96 ppm). Absence of positional isomers, namely 8- and 10-octadecynoic acids, was established analytically by ozonization and GLC determination of the monobasic and dibasic acid fragments (15). Isomerization to allene and positional acetylenes are consequently precluded in efficient dehydrohalogenations in which base is not present in large excess and reaction times are not long.

The parametric determinations offered the opportunity of devising a preparative procedure for carrying out both the bromination of oleic acid and dehydrobromination of the dihalide in 1 reaction vessel. Oleic acid was brominated in ethyl ether at -10 C. Excess bromine was almost instantaneously quenched with 2-methyl-2-butene. This compound, acting as a bromine scavenger, obviates isolation of the brominated acid that would otherwise be necessary through thiosulfate or bisulfite reduction of unreacted bromine. As formerly described in the procedure, addition of n-propanol solvant, KOH and DMSO, distillation of the

TABLE I

Conversion of 9,10-Dibromostearic Acid to 9(10)-Bromo-9-Octadecenoic and Stearolic Acids: Effects of Dimethyl Sulfoxide, Time and Temperature[a]

			Products (%)		
Temperature	DMSO-DBSA[b] (mol ratio)	Time (hr)	-C≡C-	-CH=CBr-	-CH(Br)-CH(Br)-
25 C methanol	0	1		80	20
	0	2		91	9
	0	5		99	
	20	0.25	3	97	
	20	1	7	93	
60 C in methanol	0	(5 min)		99	
	0	1	2	98	
	4	1	10	90	
	4	3	49	51	
	20	0.5	63	37	
	20	1	90	8	
	20	1.5	96	2	
100 C in n-propanol	0	2	80	20	
	0	4	92	5	
	0	5	97	2	
	3	1	89	2	
	3	2	98	2	
	5	1	95		
	5	2	98		
	20	0.25	99		

[a]KOH/DBSA = 4.
[b]DMSO = dimethyl sulfoxide; DBSA = 9,10-dibromostearic acid.

ether and low molecular weight dehydrobromination products from the scavenger and refluxing the mixture for 1 to 2 hr comprised a simple, straightforward sequence for the quantitative preparation of acetylenic acid within 3 hr. The solid stearolic acid was isolated by precipitation in ice-cold aqueous hydrochloric acid. This procedure has produced crude stearolic acid of 98-99% purity by GLC in 98-99% conversion from oleic acid. Because of its simplicity, the method should have commercial adaptability and wider scope for deriving acetylenic compounds from olefinic precursors.

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