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REDUCTION OF CONJUGATED DIENOIC CARBOXYLIC ACIDS AND ESTERS WITH SODIUM DITHIONITE

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Reduction of 2,4-alkadienoic acids and esters with sodium dithionite was carried out in aqueous solution or under PTC conditions to give, almost exclusively, Z:E isomeric mixtures of the corresponding 3-alkenoic acids and esters, respectively, in good yields.

The scope of the application of sodium dithionite as reducing agent in organic synthesis[1] has been recently extended by the use of cosolvents[2] such as DMF and dioxane, crown ethers[3] and phase transfer catalysts[4] to overcome the lack of solubility of this salt in organic solvents.

In relation to a synthetic problem arisen in our laboratory, we became interested in the study of regio- and chemoselective reduction of conjugated dienoic carboxylic acids and esters with this reagent. The reaction was carried out in aqueous solution or under phase transfer catalytic (PTC) conditions to afford a mixture of Z:E isomers of the corresponding 3-alkenoic acids and esters in good yields (Scheme 1).

Scheme 1

1 2 3

a: $R_1 = CH_3$, $R_2 = H$
b: $R_1 = C_5H_{11}$, $R_2 = H$
c: $R_1 = CH_3$, $R_2 = CH_3$
d: $R_1 = C_5H_{11}$, $R_2 = C_2H_5$
e: $R_1 = C_7H_{15}$, $R_2 = C_2H_5$
f) $R_1 = C_7H_{15}$, $R_2 = H$

Sorbic acid (1a) was chosen as model compound for this study. Preliminary assays carried out at room temperature showed that the reaction was too slow for practical use. On the other hand, high molar ratios of sodium dithionite and long reaction times decreased the yield of reduced products. As shown in Table 1, best results were obtained by running the reaction with a 1.5:2:1:1 ratio of sodium dithionite: $NaHCO_3$:NaOH:1a at 90ºC for a short time. In our standard procedure, $NaHCO_3$ and 85% commercial sodium dithionite were sequentially added under nitrogen to a vigorously stirred solution of sodium alkadienoate (prepared by neutralizing 1a with NaOH or $NaHCO_3$) at 90ºC at such a rate as to get gas evolution under control. After the given reaction time, the mixture

Likewise, reduction of conjugated dienic carboxylic esters was studied on methyl sorbate (1c) as model compound. In this case, as depicted in Table 2, best results were achieved by carrying out the reduction under PTC conditions using a 1.5:4:1.5:1 of sodium dithionite:$NaHCO_3$:Adogen 464[6]:1c molar ratio, in a benzene:water two phase system (0.5M in 1c), 1 h at 80ºC, to give after work-up (separation of the organic layer, washing the aqueous layer twice with hexane, and filtering through a SiO_2 column the joined organic fractions and eluting with hexane: diethyl ether 10:1 to 1:1) a 53:47 E:Z 2c mixture in 72% yield. Under the above GC conditions the presence of the corresponding 3c isomer could not be detected in this case. Alternative reduction in 1:1 H_2O: DMF or H_2O:dioxane afforded lower yields (50-55%) of the same isomeric mixture of 3-hexenoates, but in the former case hydrolysis occurred on increasing the reaction time. Similarly, reduction of ethyl 2,4-decadienoate (1d)[7] and ethyl 2,4-dodecadienoate (1e)[8] afforded the expected 3-alkenoates (Z:E 53:47) in 70-75% yield.

Table 2. Reduction of Conjugated Dienoate Esters with Sodium Dithionite

Substrate	R_1	R_2	$Na_2S_2O_4$:$NaHCO_3$: :Adogen:1	Solvent	Temp (ºC)	Time (h)	% Product (E:Z ratio)[a]	% Reçovd.s.m.[a]
1c	CH_3	CH_3	1.5:4:0:1	DMF:H_2O	90	1	52% 2c	
1c	CH_3	CH_3	1.5:4:1.5:1	PhH:H_2O	80	1	72% 2c(53:47)	
1c	CH_3	CH_3	1.5:4:0.1	Dioxane:H_2O	90	1	44% 2c	16% 1c
1c	CH_3	CH_3	1.5:2:0.3:1	PhH:H_2O	80	1	65% 2c(53:47)	
1c	CH_3	CH_3	1.5:4:0.3:1	PhH:H_2O	20	23	54% 2c	22% 1c
1c	CH_3	CH_3	1.5:2:0.05:1	PhH:H_2O	80	1	49% 2c	31% 1c
1c	CH_3	CH_3	1.5:2:0.05:1	PhH:H_2O	80	4	54% 2c	27% 1c
1d	C_5H_{11}	C_2H_5	1.5:4:0.3:1	PhH:H_2O	80	1	75% 2d(47:53)	
1e	C_7H_{15}	C_2H_5	1.5:4:1.5:1	PhH:H_2O	80	1	70% 2e(48:52)	

[a] By GC analysis on a SE-52 glass capillary column.

The isomeric mixture obtained by reduction of 1e was converted into the corresponding (Z/E)-3-dodecenyl acetate, which proved to be highly active in field tests as an attractant for the sugar beet moth Scrobipalpa ocellatella (Boyd) males.[9] Further work is in progress to improve the stereochemical outcome of the reaction.

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was cooled to room temperature and concentrated hydrochloric acid was added till final pH 1, which promoted a vigorous evolution of SO_2. The extraction with CH_2Cl_2 and usual work-up led to the isolation of the reduction product. GC analysis (20 m x 0.45 mm capillary column coated with a 0.1 µ film of SE-52,56ºC) of a methylated sample of the crude material showed the stereochemical outcome of the reaction.

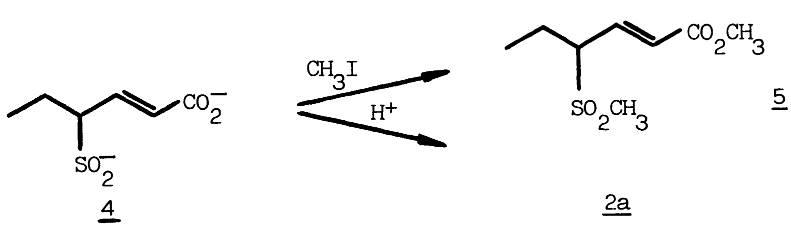
Table 1. Reduction of Conjugated Dienoic Carboxylic Acids with Sodium Dithionite

Substrate	R_1	R_2	$Na_2S_2O_4$:$NaHCO_3$:NaOH:1	Temp(°C)	Time(h)	% Product[a]	% Recovd.s.m.[a]
1a	CH_3	H	2:5:0:1	20	24	40% 2a	40% 1a
1a	CH_3	H	2:4:0:1	90	5	63% 2a 7% 3a	
1a	CH_3	H	2:2.5:0:1	90	1	57% 2a	18% 1a
1a	CH_3	H	2:2.5:0:1	90	4	68% 2a 4% 3a	
1a	CH_3	H	2:2.5:0:1	90	8	62% 2a 4% 3a	
1a	CH_3	H	1.5:4:0:1	90	0.5	56% 2a	16% 1a
1a	CH_3	H	1.5:2:1:1[b]	90	0.5	74% 2a[c] 2% 3a	
1b	C_5H_{11}	H	1.5:2:1:1	90	1	69% 2b[c]	9% 1b

[a] By GC analysis of the methyl ester on a SE-52 glass capillary column.[5]
[b] Sodium dithionite was added in three portions at ten minutes interval.
[c] E:Z ratio 72:28.

To gain some insight on the mechanism of this reaction, the aqueous solution from the reduction of 1a was evaporated prior to the acidification. A ^1H-NMR spectrum run on the residue in D_2O showed main absorptions at δ 6.3 (dd, J= 16 Hz, 9 Hz, 1H), 5.9 (d, J= 16 Hz, 1H), 2.7 (complex, 2H) and 0.9 (t, J=8 Hz, 3H), consistent with the formation of compound 4 as intermediate and precursor of 3-alkenoic acids (3), plausibly *via* prototropic shift with concomitant loss of SO_2 on acidification (Scheme 2).

Scheme 2



Structure 4 was further confirmed by treatment of the above residue with CH_3I in refluxing MeOH to give the sulfone ester 5 characterized by spectral means: ^1H-NMR ($CDCl_3$) δ 6.8 (dd, 16 Hz, 9 Hz, 1H), 6.2 (d, J=16 Hz, 1H), 3.8 (s, 3H), 3.4 (complex, 1H), 2.9 (s, 3H), 1.8 (complex, H), 1.0 (t, J=7 Hz, 3H).

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5. The compounds were identified by comparison with authentic samples as follows: E-2a with the acid prepared by an independent procedure according to A. J. Birch and J. Slobbe; Aust. J. Chem., 2737 (1976); Z-2a via LAH reduction of the methyl ester with Z-3-hexenol (Firmenich); acid 3a was identified by GC-MS of the corresponding 3c ("Registry of Mass Spectral Data", ed. E. Stenhagen, S. Abrahamsson and F. W. Mc Lafferty, Vol. 1, 1974) and assigned the E stereochemistry.
6. Adogen 464 is a commercial mixture of methyl trialkyl (C_8-C_{10}) ammonium chlorides.
7. Ester 1d was obtained through a generous gift from GIVAUDAN and its stereochemistry shown to be E,E 30%, E,Z 69%, Z,E 1% by GC analysis on a 3 m x 1/8" glass column, 5% FFAP on Chrom.W.
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