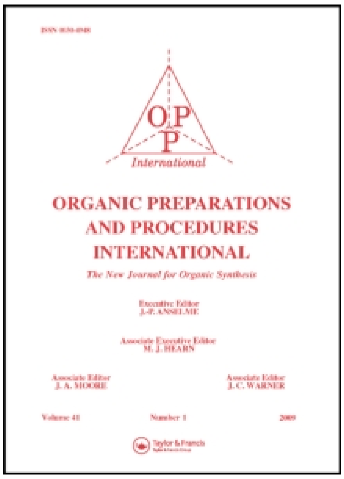

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PREPARATION OF ω-BROMOALKAN-1-OLS FROM α,ω-ALKANEDIOLS BY THE CONTINUOUS EXTRACTION METHOD

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Conversion of symmetrical α,ω-alkanediols into the corresponding ω-haloalkan-1-ols is a basic reaction for preparation of intermediates in the synthesis of pheromones.[1] This transformation has been conducted mainly on a small scale by application of the solid phase synthesis procedure,[2] by selective formation of alkoxyphosphonium salts[3] or by use of the continuous extraction method in large scale preparations.[4] However, to our knowledge, a systematic study of the reaction conditions to optimize the latter procedure has not been undertaken. Moreover, the application of the reaction to the preparation of 4-bromobutan-1-ol and 5-bromopentan-1-ol has, surprisingly, not been described. We report herein the results of our study for the complete series of α,ω-alkanediols from n = 4 to n = 10. In addition we have used one of the compounds prepared, 10-bromohexan-1-ol, for the synthesis of (Z)-13-hexadecen-11-ynyl acetate, a major component of the sex pheromone of the processionary moth *Thaumetopoea pityocampa* (Denis and Schiff.) (Lepidoptera, Notodontidae).[5-7]

$$\mathrm{HO(CH_2)_nOH} \quad + \quad \mathrm{HBr} \longrightarrow \mathrm{HO(CH_2)_nBr} \qquad n = 4\text{-}10$$

The reaction was carried out by heating a mixture of 48% aqueous HBr and the diol in a given ratio, in a continuous extraction system using n-heptane as solvent, except for n = 4 where toluene was more suitable. Analysis of an aliquot of the reaction mixture allowed us to monitor the progress of the conversion of the diol into the desired ω-bromoalkan-1-ol (GLC on OV-101 column); the results are summarized in Table 1.

TABLE 1. Formation of ω-Bromoalkan-1-ols from α,ω-Alkanediols[a]

Entry	n	Molar Ratio Diol:HBr	Time (hrs)	Crude Yield(%)	GC Anal.[b]	Distilled Product(%)
1	4	1:3	40	27	86:14	--
2	4	1:6	14	32	53:47	--
3	4	1:3[c]	7	38	68:32	--
4	4	1:3[c,d]	168	58	99:1	e
5	5	1:1.5	86	47	92:8	--
6	5	1:3	86	66	94.6	60
7	6	1:3	63	91	95:5	83
8	7	1:3	87	83	95:5	80
9	8	1:3	64	92	95:5	85
10	9	1:3	86	86	97:3	77
11	9	1:6	24	98	98:2	82
12	10	1:6[f]	24	40	95:5	--
13	10	1:9	24	87	98:2	--
14	10	1:12	24	90	92:8	79

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a. Solvent is heptane and temperature 80° unless otherwise noted. b. Ratio of monobromo:dibromo derivative. c. Solvent: toluene. d. 40°.
e. The crude 4-bromobutan-1-ol obtained was chromatographically and spectroscopically pure, however, attempts to distil this material, even in the presence of sodium carbonate, did not yield the expected product, probably due to cyclization to tetrahydrofuran. f. 92°.

It must be emphasized that this procedure is especially convenient for the preparation of 5-bromopentan-1-ol (normally prepared by more complex and/or longer methods[8]) from readily accessible materials. Yields for $n \geqslant 6$ were generally higher than 80% of distilled material and purity better than 95% was achieved.

EXPERIMENTAL SECTION

Gas chromatographic analyses were performed on a Carlo Erba Fractovap 2350 gas chromatograph equipped with a flame ionization detector using 3% OV-101 and 5% FFAP on Chromosorb W 2m x 1/8" glass columns, operating at a nitrogen flow rate of 18 ml/min. Diols were purchased from commercial sources and were used without further purification. IR spectra were recorded in carbon tetrachloride on Perkin Elmer 257 and 399B spectrometers and absorptions are expressed in cm^{-1}. ^{1}H NMR spectra were recorded in carbon tetrachloride or deuteriochloroform on a Perkin Elmer R12B instrument operating at 60 MHz and values are expressed in δ scale relative to TMS. ^{13}C NMR spectra were taken in deuteriochloroform using TMS as internal standard on a Bruker WP80SY spectrometer. The signals, in ppm, were assigned by comparison with calculated values (in parenthesis).

TABLE 2. Physical and Spectral Data of ω-Bromoalkan-1-ols

Compound bp. (lit.)°C	IR	^{1}H nmr	^{13}C nmr
$Br(CH_2)_4OH$ -- (56-8°/2 mm)[9a]	3620 3340 1055 645	3.60 (t, 3H J=6.0 Hz, CH_2Br) 3.40 (t, 3H J=6.5 Hz, CH_2OH) 2.15 (s, 1H, OH) 2.3-1.2 (m, 4H, CH_2CH_2)	C_1 61.5(61.5), C_2 30.8 (30.8), C_3 29.1(28.8), C_4 33.4(33.0).
$Br(CH_2)_5OH$ 47-50°/0.05 mm (117°/20 mm)[8b]	3620 3340 1050 640	3.52 (t, 3H J=6.0 Hz, CH_2Br) 3.35 (t, 3H J=6.5 Hz, CH_2OH) 4.60 (s, 1H, OH) 2.25-1.15 (m, 6H, CCH_2C)	C_1 62.3(62.8), C_2 31.3 (31.6), C_3 24.2(24.8), C_4 32.3(32.1), C_5 33.4 (34.3).
$Br(CH_2)_6OH$ 60-2°/0.03 mm (105-6°/5 mm)[11]	3625 3320 1050 640	4.26 (s, 1H, OH) 3.50 (t, 3H J=6.0 Hz, CH_2Br) 3.40 (t, 3H J=6.5 Hz, CH_2OH) 2.1-1.15 (m, 8H, CCH_2C)	C_1 62.3(62.7), C_2 32.2 (32.7), C_3 24.7(25.3), C_4 27.7(27.8), C_5 32.5 (32.7), C_6 33.5(32.7).
$Br(CH_2)_7OH$ 76-8°/0.25 mm (108°/1 mm)[8b]	3630 3330 1060 650	3.70 (s, 1H, OH) 3.50 (t, 3H J=6.0, CH_2Br) 3.25 (t, 3H J=6.5 Hz, CH_2OH) 2.1-1.2 (m, 10H, CCH_2C)	C_1 62.6(62.8), C_2 32.4 (32.6), C_3 25.5(26.6), C_4 28.0(28.3), C_5 28.4 (28.6), C_6 32.6(32.6), C_7 33.7(33.7).
$Br(CH_2)_8OH$ 81°/0.06 mm (79°/0.07 mm)[12]	3625 3330 1055 650	4.03 (s, 1H, OH) 3.45 (t, 3H J=6.0 Hz, CH_2Br) 3.32 (t, 3H J=6.5 Hz, CH_2OH) 2.1-1.1 (m, 12H, CCH_2C)	C_1 62.2(62.8), C_2 32.2 (32.6), C_3 25.4(26.4), C_4 28.9(29.9), C_5 28.4 (29.1), C_6 27.8(28.4) C_7 32.5(32.6), C_8 33.5 (33.7).
$Br(CH_2)_9OH$ 90-2°/0.07 mm (113°/0.7 mm)[4a]	3630 3340 1055 650	3.60 (s, 1H, OH) 3.55 (t, 3H J=6.0 Hz, CH_2Br) 3.35 (t, 3H J=6.5 Hz, CH_2OH) 2.2-1.1 (m, 14H, CCH_2C)	C_1 61.7(62.8), C_2 32.1 (32.6), C_3 25.2(26.4), C_4 28.8(30.4), C_5 28.8 (29.4), C_6 28.1(28.9), C_7 27.6(28.4), C_8 32.3 (32.6), C_9 33.1(33.7).
$Br(CH_2)_{10}OH$ 99-101°/0.07 mm (169°/10 mm)[13]	3630 3340 1050 650	2.65 (s, 1H, OH) 3.50 (t, 3H J=6.0 Hz, CH_2Br) 3.32 (t, 3H J=6.5 Hz, CH_2OH) 2.2-1.1 (m, 16H, CCH_2C)	C_1 62.5(62.9), C_2 32.6 (32.8), C_3 25.6(26.6), C_4 29.2(29.7), C_5 29.2 (30.1), C_6 29.2(30.1), C_7 28.5(29.2), C_8 28.0 (28.2), C_9 32.6(32.8), C_{10} 33.5(33.7).

Reaction of α,ω-Alkanediols with 48% Hydrobromic Acid. Preparation of 5--Bromopentan-1-ol as Representative Procedure (Entry 6).- In a continuous liquid-liquid extraction system of 250 ml capacity, similar to that described,[10] were placed 7.70 g. (74 mmoles) of 1,5-pentanediol, 25 ml of 48%

HBr (222 mmoles) and 225 ml of n-heptane. In the distilling flask were refluxed 200 ml of n-heptane so that the condensing solvent passing through the internal funnel bubbled into the aqueous phase,thus allowing extraction of the brominated compound and preventing the formation of the corresponding dihalide. The internal funnel was sealed in the form of a small bulb with twelve 1-2 mm holes and rested on the bottom of the flask. The aqueous layer was maintained at 80° (bath temperature) and the distilling flask was kept at 120-130° (bath temperature) so that a total of 100-200 bubbles per minute passed through the reaction mixture. The solvent was renewed every 24 h until no significant amount of organic material was recovered. The organic phases were combined, washed with saturated sodium bicarbonate solution and dried over magnesium sulfate. The solvent was removed under vacuum to leave a residue which after distillation at reduced pressure (47-50°/0.05 mm) yielded 7.44 g. (60%) of 5-bromopentan-1-ol, contaminated with 6% of the corresponding 1,5-dibromopentane (retention time 5.1 min. at 110° column temperature on OV-101 3% on Chromosorb W).

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AN IMPROVED PROCEDURE FOR THE OXIDATION OF 2,5- AND 5,6-DIHALO-3-METHYLPYRIDINES

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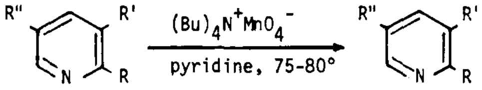
Oxidations of 2,5- and 5,6- dihalo-3-methylpyridines to the respective 2,5- and 5,6- dihalonicotinic acids with aqueous potassium permanganate proceed in low yields (10-50%)[1-5]. The use of tetrabutylammonium permanganate (TBAP) in pyridine[6] significantly improves the yields of the aforementioned oxidations (Table 1).

I



II

a) R = Cl; R' = Br; R" = CH_3
b) R = Br; R' = Br; R" = CH_3
c) R = Br; R' = CH_3; R" = I
d) R = Cl; R' = CH_3; R" = Br
e) R = Br; R' = CH_3; R" = Br
f) R = F; R' = CH_3; R" = Br
g) R = Cl; R' = CH_3; R" = I
h) R = Br; R' = CH_3; R" = Cl

a) R = Cl; R' = Br; R" = COOH
b) R = Br; R' = Br; R" = COOH
c) R = Br; R' = COOH; R" = I
d) R = Cl; R' = COOH; R" = Br
e) R = Br; R' = COOH; R" = Br
f) R = F; R' = COOH; R" = Br
g) R = Cl; R' = COOH; R" = I
h) R = Br; R' = COOH; R" = Cl

Table 1. Comparative Yields (%) of Nicotinic Acids (II) from Oxidations

Method	IIa	IIb	IIc	IId	IIe	IIf	IIg	IIh
$KMnO_4$	50[1]	45[1]	16[5]	25[1]	30[1]	28[1]	30[4]	43[5]
TBAP	62	72	66	61	64	73	72	60