Selective Monoprotection of the Less Alkylated Double Bond in Dienes

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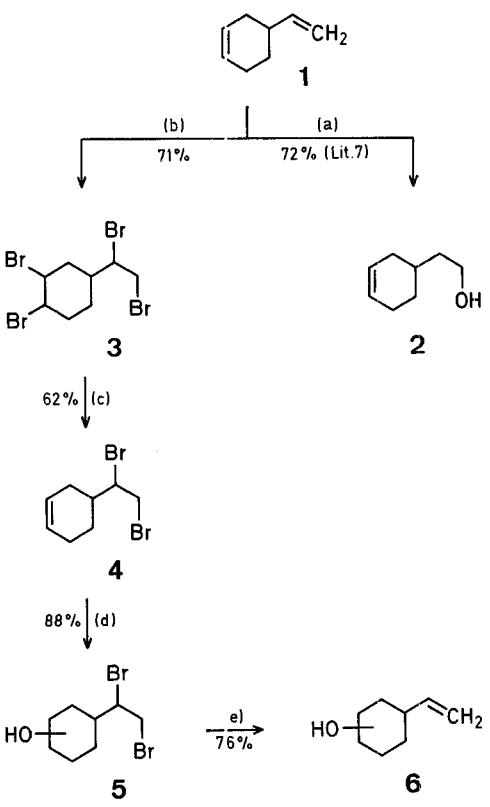
Vicinal dibromides can be cathodically converted into olefins[1]. Their reduction potential is shifted to more anodic values[2] with increasing alkylation. This opens a route to selective monoprotection of the less alkylated double bond in dienes. The diene is converted into the tetrabromide with bromine or pyridinium hydrobromide perbromide[3] and subsequently monodeprotected at the higher alkylated double bond by controlled-potential electrolysis. To our knowledge, potential-selective debrominations of tetrabromides have not yet been reported. By this method, the "overlap-controlled" olefin additions[4], for example hydroboration or diimide reduction, which preferentially take place at the less alkylated olefinic site[5,6], can be forced to proceed selectively at the higher alkylated double bond. This has been proven by the hydroboration/oxidation of 4-vinylcyclohexene (**1**). Hydroboration of **1** with disiamylborane and oxidative work-up affords 72% 2-(3-cyclohexenyl)-ethanol (**2**)[7]. On the other hand, the selective hydroboration of the disubstituted double bond to give **6** is achieved by conversion of **1** to the tetrabromide **3** and cathodic reduction of **3** at −1.4 V (vs. sce) to give the dibromide **4**; hydroboration/oxidation of **4** affords the dibromoalcohol **5** which is debrominated by cathodic reduction at −1.8 V (vs. sce) to give the isomeric vinylcyclohexanols **6**[8].



Reaction conditions:

(a) 1. $(C_5H_{11})_2BH$ (disiamylborane)/tetrahydrofuran; 2. NaOH/H_2O_2/H_2O.

(b) Method A: Br_2/tetrachloromethane, −10° to −40°; Method B: Br_2/ether (12)/isobutanol (1), −10° to −40°; Method C:

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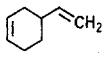
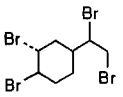
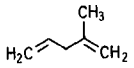
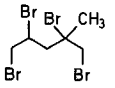
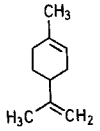
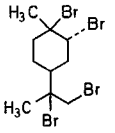
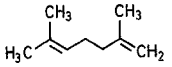
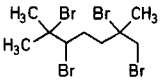
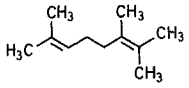
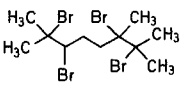
Table 1. Tetrabromoalkanes from Non-conjugated Dienes; Reaction (b)

Diene	Bromination Method	Tetrabromoalkane	Yield[a] [%]	Physical Data	Molecular formula[b] or Lit. data	^{1}H-N.M.R. (CCl_4/TMS) δ [ppm]
 1	A	 3	71	m.p. 72–73° (ether)	m.p. 77.4–88.3°[8]	1.4–2.85 (m, 7H, CH_2, CH); 3.78 (m, 2H, CH_2Br); 4.18 (m, 1H, CHBr); 4.68 (m, 2H, CHBr CHBr)
	C	 7	99	b.p. 100°/0.3 torr[c]	$C_6H_{10}Br_4$ (401.7)	1.98–2.06 (2 s, 3H, CH_3); 2.67 (m, 2H, CH_2); 3.9 (m, 4H, CH_2Br); 4.46 (m, 1H, CHBr)
	B	 8	46	m.p. 102–103° (ethanol/ether)	m.p. 104–105°[9]	1.65–2.35 (m, 12H, CH_2, CH_3); 2.58 (m, 1H, CH); 3.76, 3.88 (2 d, J = 10 Hz, CH_2Br); 4.65 (m, 1H, CHBr)[9]
	D	 9	91	n_D^{20} = 1.5630	$C_9H_{16}Br_4$ (443.8)	1.8–2.9 (m, 13H, CH_3, CH_2); 3.86 (s, 2H, CH_2Br); 4.17 (m, 1H, CHBr)
	D	 10	86	m.p. 116 (ethanol/ether)	$C_{11}H_{20}Br_4$ (471.9)	1.8–3.0 (m, 19H, CH_2, CH_3); 4.18 (m, 1H, CHBr)

[a] Yield of isolated, purified product.
[b] The microanalyses of the new compounds were in satisfactory agreement with the calculated values: C, ±0.22; H, ±0.28; Br, ±0.35.
[c] By bulb-to-bulb distillation.

pyridinium hydrobromide perbromide/chloroform, room temperature; Method D: pyridinium hydrobromide perbromide/chloroform, −60°.

(c) Hg cathode, −1.4 V (vs. sce)/dimethylformamide/tetrabutylammonium tetrafluoroborate.

(d) 1. B_2H_6/tetrahydrofuran; 2. $NaOH/H_2O_2/H_2O$.

(e) Hg cathode, −1.8 V (vs. sce)/dimethylformamide/tetrabutylammonium tetrafluoroborate.

Data of **6**:

$C_8H_{14}O$ (126.2) calc. C 76.14 H 11.18 found 76.19 11.19

M.S.: m/e = 126 (M^+, 0.25%); 108 (34); 93 (82); 79 (100); 67 (42).

I.R. (film): ν = 3330 (broad); 3068; 1638; 1045; 995; 910 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6): δ = 0.7–2.6 (m, 9H, CH_2, CH); 3.6 (m, 1H, CH—OH); 4.32 (m, 1H, CH—OH); 4.93 (m, 2H, $=CH_2$); 5.76 ppm (m, 1H, —CH=).

Scope and selectivity of this monoprotection are demonstrated by the examples given in the Tables. Representative non-conjugated dienes with different substitution at the double bonds were converted to the tetrabromides (Table 1) and these were potential-selectively reduced to the dibromides (Table 2).

Tetrabromoalkanes by Bromine Addition to Non-conjugated Dienes [Reaction (b), Methods C, D]; General Procedure:

Pyridinium hydrobromide perbromide (8 g, ~25 mmol) is added to a stirred solution of the diene (10 mmol) in chloroform (30 ml) at −60°. The mixture is stirred at −60° for 2 h [in the case of 2-methyl-1,4-pentadiene at 25° for 4 h; at −60°, only the dialkylated double bond is brominated (80% yield of isolated product)]. The mixture is allowed to warm to 0° and excess brominating agent is destroyed by the addition of aqueous sodium hydrogen sulfite. The mixture is then washed with water (3 × 30 ml) and dried with magnesium sulfate. The solvent is evaporated in vacuo (~20 and 0.05 torr). The residual product is >95% pure and may be electrolyzed without further purification. The crude product may be purified by recrystallization or column chromatography on silica gel using petroleum ether as solvent.

Controlled-Potential Reduction (Selective Debromination) of the Tetrabromoalkanes 3, 7, 8, 9, 10:

The reaction is carried out in a divided beaker-type glass cell with a cooling jacket; mercury pool cathode; platinum anode; catholyte: the tetrabromoalkane (5–10 mmol) in a 0.1 molar solution of tetrabutylammonium tetrafluoroborate in dimethylformamide (20–40 ml); anolyte: 0.1 molar solution of tetrabutylammonium tetrafluoroborate in dimethylformamide (6–12 ml) containing sodium carbonate (0.2 g). The reduction is performed with slight stirring at a controlled potential (Table 2) and an initial current of 100–300 mA. Upon complete debromination of one double bond (monodeprotection), the current decreases to 10–20 mA and the electrolysis is stopped. The catholyte is poured into water (120 ml), the solution extracted with ether (5 × 70 ml), the extracts washed with water (2 × 50 ml), dried with magnesium sulfate, evaporated, and the residual product purified by distillation or preparative layer chromatography (P.L.C.) on silica gel using petroleum ether as solvent.

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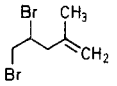
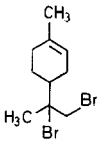
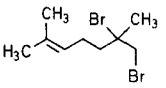
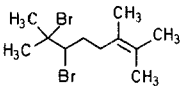
Table 2. Dibromoalkenes by Controlled-Potential Reduction of Tetrabromoalkanes; Reaction (c)

Tetrabromoalkane	Reduction potentials [V] (vs. sce) from polarography[a] (applied in controlled-potential electrolysis)	Dibromoalkene		Yield[b] [%]	Selectivity[c] [%]	Physical Data	Molecular formula[d]	^{1}H-N.M.R. (CCl_4/TMS) δ [ppm]
3	−1.25, −1.58 (−1.3)	4		62	96	m.p. 39–40°	$C_8H_{12}Br_2$ (268.0)	1.3–2.4 (m, 7H, CH_2, CH_3); 3.73 (m, 2H, CH_2Br); 4.2 (m, 1H, CHBr); 5.65 (m, 2H, CH=)
7	−0.97, −1.65 (−0.9)	11		76	95	b.p. 90–100°/ 15 torr[e]	$C_6H_{10}Br_2$ (242.0)	1.82 (s, 3H, CH_3); 2.41, 3.0 (2 m, 2H, CH_2); 3.58, 3.87 (2 m, 2H, CH_2Br); 4.2 (m, 1H, CHBr); 4.89 (m, 2H, CH_2)
8	−0.83, −1.38 (−1.0)	12		48	96	b.p. 85–87°/ 50 torr[e] (m.p. 27°)[9]		1.4–2.3 (m, 13H, CH, CH_2, CH_3); 3.72, 3.89 (2 d, J = 10 Hz, 2H, CH_2Br); 5.34 (m, 1H, CH=)[9]
9	−0.8 to −1.7[f] (−0.8)	13		61	93	n_D^{20}: 1.5137	$C_9H_{16}Br_2$ (284.0)	1.5–2.4 (m, 13H, CH_2, CH_3); 3.75, 3.89 (2 d, J = 10 Hz, 2H, CH_2Br); 5.15 (m, 1H, CH=)
10	−0.39; −0.72; −1.24 (−0.6)	14		79	>95[g]	n_D^{20}: 1.5141	$C_{11}H_{20}Br_2$ (312.1)	1.6–2.75 (m, 19H, CH_3, CH_2); 4.1 (d of d, J = 10.5 Hz, J = 1.5 Hz, 1H, CHBr)

[a] Differential pulse chromatography; drop time: 1 sec, sweep rate: 10 mV/sec, pulse amplitude: 50 mV; 0.001 molar solution in dimethylformamide, 0.1 molar tetrabutylammonium tetrafluoroborate.

[b] Yield of isolated pure product.

[c] The less alkylated *vic*-dibromoalkyl moiety is debrominated only to a small extent. The selectivities given refer to debromination at the higher alkylated site of the tetrabromoalkane, i.e., to the percentage of the pure dibromoalkenes listed in the debromination product. The selectivity was determined by G.L.C. analysis (4% SE 30 on Chromosorb W).

[d] The microanalyses of the new products were in satisfactory agreement with the calculated values: C, ±0.24; H, ±0.06; Br, ±0.38.

[e] By bulb-to-bulb distillation.

[f] Broad unresolved peak.

[g] G.L.C. analysis was not possible. The isomeric dibromoalkene could not be detected by ^{1}H-N.M.R. analysis.

Prof. Dr. W. Lüttke dedicated to his 60th birthday.

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