Selective Monoprotection of the Higher Alkylated Double Bond in Dienes by Bromination

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Selective monofunctionalization of dienes is possible by blocking one of the double bonds. However, only few

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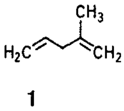
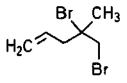
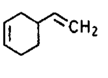
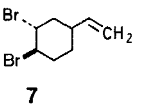
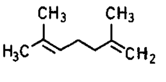
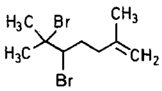
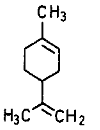
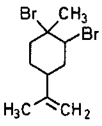
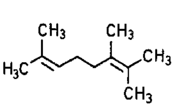
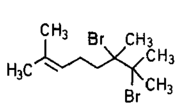
Table. Selective Bromine Addition to the Higher Alkylated Double Bond of Dienes using Pyridinium Hydrobromide Perbromide

Diene[a]		Dibromide	Yield [%]	Selectivity[b] [%]	b.p./torr	Molecular formula[c]	^{1}H-N.M.R. (CCl_4/TMS) δ [ppm]
 **1**	→	 **6**	83	100	60–70°/0.7[d]	$C_6H_{10}Br_2$ (242.0)	1.88 (s, 3H, CH$_3$); 2.65 (d, 2H, CH$_2$, J=6.5 Hz); 3.81 (s, 2H, CH$_2$Br); 5.2 (m, 2H, CH$_2$); 5.88 (m, 1H, CH)
 **2**	→	 **7**	75	99	50–60°/0.02[e]		1.6–2.8 (m, 7H, CH$_2$, CH); 4.65 (m, 2H, CHBr CHBr); 5.03 (m, 2H, CH$_2$); 5.76 (m, 1H, CH)
 **3**	→	 **8**	78[f]	100	60–70°/ 0.01–0.05[d]	$C_9H_{16}Br_2$ (284.0)	1.7–2.5 (m, 13H, CH$_2$, CH$_3$); 4.15 (2 m, 1H; CHBr); 4.76 (m, 2H, CH$_2$)[7]
 **4**	→	 **9**	55	98	70–80°/ 0.01–0.05[d]	$C_{10}H_{16}Br_2$ (296.1)	1.6–2.62 (m, 13H, CH$_2$, CH$_3$); 4.69 (m, 1H, CHBr); 4.76 (s, 2H, CH$_2$)
 **5**	→	 **10**	[g]	>95[h]		$C_{11}H_{20}Br_2$[i] (312.1)	1.58–2.4 (m, 19H, CH$_3$, CH$_2$); 5.1 (m, 1H, CH)

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[a] The dienes **3** and **5** were obtained from 6-methyl-5-hepten-2-one by Wittig reaction with methylene- or isopropylidenetriphenylphosphorane, respectively. The other dienes were obtained from commercial sources.

[b] The less alkylated double bond is only brominated to a small extent. The selectivity (% of main isomer) was determined by G.L.C. (4% SE 30 on Chromosorb W).

[c] The microanalyses of products **6–9** showed the following maximum deviations from the calculated values: C, ±0.21; H, ±0.20; Br, +0.41.

[d] Determined by bulb-to-bulb distillation.

[e] Ref. [8], b.p. 64–79.5°/3 torr.

[f] A 40% yield of analytically pure product **8** (distilled in moderate vacuum) has been obtained from diene **3** and elemental bromine by Schlosser and Chau[7].

[g] Compound **10** could not be isolated in a pure form; yield of 6,7-epoxy-2,3,7-trimethyl-2-octene obtained after epoxidation and cathodic debromination: 36%.

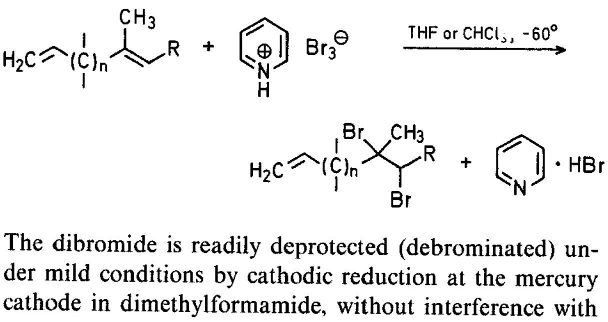
[h] The isomeric dibromide could not be detected by ^{1}H-N.M.R. analysis; G.L.C. analysis was not possible.

[i] Microanalysis was not possible. Therefore microanalysis of 6,7-epoxy-2,3,4-trimethyl-2-octene:

$C_{11}H_{20}O$	calc.	C 78.51	H 11.98
(168.3)	found	78.58	12.02

dienes have so far been monoprotected selectively, for example, by Diels-Alder reaction[1], by template-directed epoxidation[2], and by complex formation with $[(C_5H_5)Fe(CO)_2]^{\oplus}$[3]. These methods suffer from the disadvantage of long reaction times, high reaction temperatures, and the partially difficult preparation of the protecting reagent.

Olefins can be protected by halogenation and reductive dehalogenation[4]. The rate of the addition of bromine rises with increasing alkylation of the double bond; the relative addition constants are (for mono-:di-:tri-:tetra-substituted double bonds) 1:60:2000:20000[5]. Due to these different reactivities, the disubstituted double bond in 4-vinylcyclohexene may be selectively blocked[6]. With pyridinium hydrobromide perbromide as reagent, the yields and the selectivities are higher than with bromine. With representative combinations of differently alkylated double bonds in dienes, the broad scope and the selectivity of this monoprotection is demonstrated. Dibromination of the diene is cleanly and simply achieved at −60° with an equimolar amount of pyridinium hydrobromide perbromide in tetrahydrofuran or chloroform.



The dibromide is readily deprotected (debrominated) under mild conditions by cathodic reduction at the mercury cathode in dimethylformamide, without interference with functional groups such as epoxide or acetal moieties[6].

Dibromoalkenes of the Type $C{=}C{-}C_n{-}CBr{-}CBr$ by Selective Bromination of Dienes; General Procedure:

Pyridinium hydrobromide perbromide (3.2 g, 10 mmol) is added over 10 min to a stirred, cooled (−60°) solution of the diene (10 mmol) in tetrahydrofuran (**2**, **4**) or chloroform (**1**, **3**, **5**) (20 ml). Stirring is continued for 1–3 h at −60°. Tetrahydrofuran is then evaporated, water (30 ml) is added and the mixture is extracted with pentane (5 × 20 ml). In contrast, the chloroform solution is washed with water (3 × 20 ml), dried with magnesium sulfate, and the solvent evaporated. The residual crude product is purified by bulb-to-bulb distillation in vacuo.

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

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