

SELECTIVE BROMINATION OF POLYOLEFINS¹

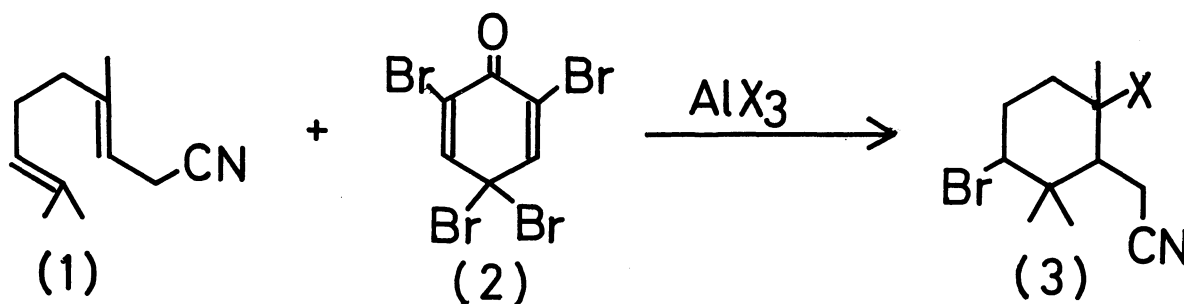
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Although the reaction mechanism is obscure at present, 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (2) was found to be a good reagent for the selective bromination of polyenes, that is, terminal double bond of geranyl and farnesyl cyanides was selectively brominated by merely being stirred with equimolar amount of 2 in CH₂Cl₂ solution, giving 6,7-dibromogeranyl (yield 98%) and 10,11-dibromofarnesyl (yield 65%) cyanide, respectively.

Directed toward the biogenetic type synthesis of halogen containing cyclic terpenoids², which might be biosynthesized by the participation of halogen cation to the terminal double bond of prenyl precursors, we have searched for a new reagent system which promises the realization of this type of reaction. Our recent research³ revealed that the brominative cyclization of model polyene (1) was effectively achieved by 2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one (2) in a biogenetic type fashion when geranyl cyanide (1) was treated with the bromoketone in the presence of AlCl₃ or AlBr₃.



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By this reaction, however, the halogenated product (3) was isolated in relatively low yield (ca 16%). In order to increase the yield of the product, we examined the chemical property⁴ of the tetrabromoketone (2) toward the polyenes under several conditions and the results will be discussed in this paper.

Table. Formation ratio of 4 and 5 under different conditions

experiment No.	Conditions ^a				Products(%)		
	Solvent(s)	mol ratio of <u>2</u> vs <u>1</u>	Additive ^b	Reaction time (hr)	<u>4</u>	<u>5</u>	Recovered (<u>1</u>)
1	DMSO+CH ₂ Cl ₂ (50:20) ^c	1	LiBr (1)	1	51	10	16
2	CH ₂ Cl ₂	2	DMSO (4) + NaBr (2)	3	64	35	0
3	DMSO+CH ₂ Cl ₂ (50:20) ^c	2		1	18	17	22
4	DMSO+CH ₂ Cl ₂ (50:20) ^c	1		1	4	30	64
5	CH ₂ Cl ₂	2	DMSO (20)	1.5	29	51	0
6	CH ₂ Cl ₂	1	DMSO (10)	6	35	4	22
7	CH ₂ Cl ₂	1		1	98	0	0

a. All the reactions were carried out at 0~25°C.

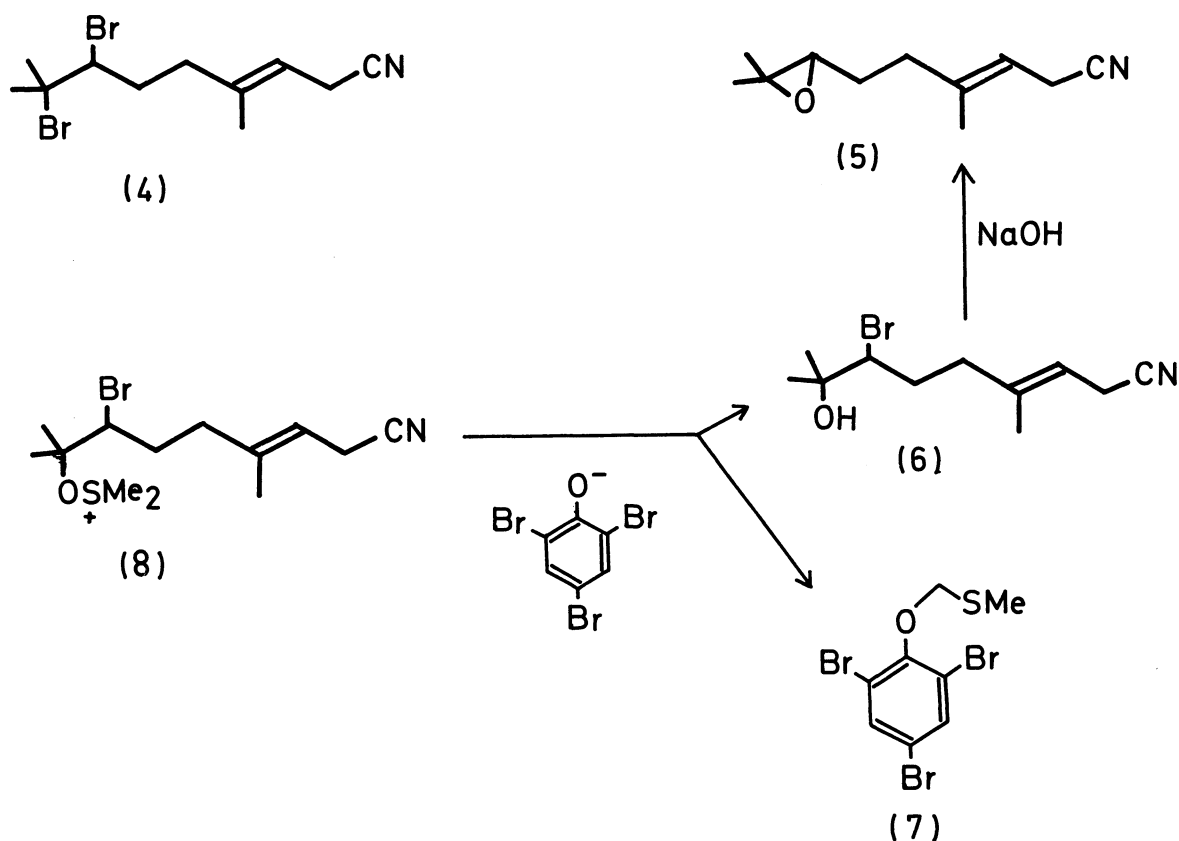
b. Number in parentheses shows the mol ratio of the additive(s) vs 1.

c. Ratio shows V/V.

In the reaction of geranyl cyanide (1) with tetrabromoketone (2), 6,7-dibromogeranyl cyanide (4) and 6,7-epoxy derivative (5) were isolated. The reaction was decisively dependent on the additives and, in addition to 4 and 5, formation of methyl (2,4,6-tribromophenoxy)methyl sulfide (7) was accompanied in various yields when DMSO was added to the reaction system⁵ (exp. No.1~No.6). The epoxide (5) is presumably derived from the initially formed bromohydrin (6) during working up the reaction mixture with aqueous NaOH, which was used to remove the resultant tribromophenol and other acidic materials. The authentic bromohydrin (6) was in fact quantitatively converted to 5 under the same conditions. These results as well as Dalton's demonstration⁶ on the formation mechanism of bromohydrin in moist DMSO strongly suggest that the origin of the oxygen atom of 6 arised from DMSO which reacted with the initially formed carbonium ion giving a sulfonium intermediate (8).⁷ Attack of tribromophenol then readily gave 6 and 7.

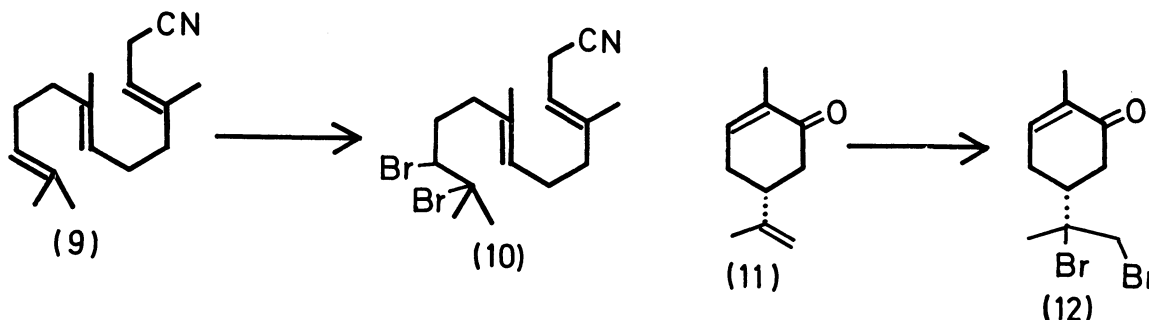
The structure of dibromo derivative (4) was confirmed by transformation to the starting material (1) with zinc in acetic acid, and supported satisfactorily by physical evidence. 4; NMR(CDCl₃) δ 1.74(3H, bs, C₄-Me), 1.82 and 1.98(each 3H, C₈-Me₂), 3.01(2H, d, 7, -CH₂CN), 4.09(1H, dd, 10 and 1.5, -CHBr-), and 5.29(1H, t, 7, =CH-)ppm. As might be expected, relative yield of 4 increased when LiBr or NaBr was added to the reaction mixture (exp. No.1 and 2). Unexpectedly, however, formation of considerable amounts of dibromide (4) was observed even though MBr(M = Li or Na) was not added to the reaction mixture (exp. No.3~No.6) and it was finally found that geranyl cyanide was quantitatively and selectively brominated when equimolar amounts of 1 and 2 were merely stirred in CH₂Cl₂ at room temperature. In the exp. No.7, large amounts of unidentified polymeric materials were formed while only little amounts of tribromophenol were detected in the acidic part.

Although the resultant polymeric materials from the reaction is not clarified at present and the bromination mechanism remains unsolved, this reaction is expected to be synthetically useful for the bromination of olefins. In fact, our preliminary experiment revealed that farnesyl cyanide (9) is brominated at the terminal double bond to give 10 in 65% yield. Similarly, carvone (11) was converted to 12 in 60%



Yield by stirring at room temperature for 2 days.

These results promise that the tetrabromoketone (2) in CH_2Cl_2 is a new and selective bromination reagent of polyfunctional olefins. 10; NMR(CCl_4) δ 1.66(bs, 3H x 2), 1.81 and 1.97(each 3H, s, $-\text{BrCMe}_2$), 3.03(2H, d, 7, CH_2CN), 4.12(1H, dd, 11 and 1.5, $-\text{BrCH}-$) and 5.18(2H, t, 7, $\text{C}=\text{CH}-$)ppm. 12; NMR(CCl_4) 1.75(3H, bd, 1.5), 1.92(3H, s), 3.78, 3.82 and 3.95[total 2H, d, 10, $-\text{CH}_2\text{Br}$ (mixture of diastereomeric isomers)] and 6.63(1H, m).



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5. Structure of 7 was confirmed by physical evidence. Anal. Calcd for $\text{C}_8\text{H}_7\text{Br}_3\text{OS}$: C, 24.58; H, 1.80. Found: C, 24.71; H, 1.59. NMR(CDCl_3) 2.40(3H, s), 5.19(2H, s), and 7.68(2H, s).
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(Received November 13, 1975)