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A GEM-ALLYL DIANION SYNTHON IN WATER

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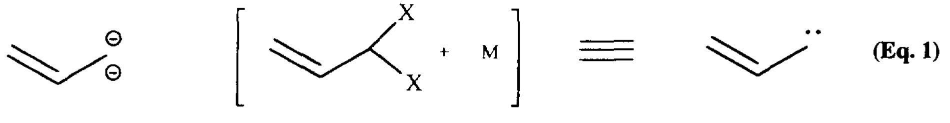
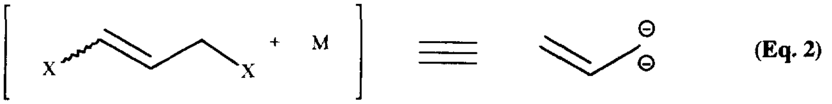
Summary: *The reaction of 1,3-dibromopropene with carbonyl compounds mediated by indium in water gave bis-allylation products connected to the same carbon. Such a reactivity effectively constitutes a gem-allyl dianion synthon.*

The synthetic versatility of various dianions and their equivalents has been a fascinating subject. Their importance and the wealth of chemistry associated with them are demonstrated by the existence of a monograph devoted to them.[1] Among the various forms of dianions, the generation of gem-allyl dianion **1** would prove considerably difficult,[2] inasmuch as 3,3-allyl dihalides **2** would normally react with reducing reagents, providing allyl carbene **3**, instead of forming an allyl dianion. Synthetically, such a synthon could provide a rapid entry to substituted 1,3-diols.[3]



1 **2** **3** **(Eq. 1)**

During the synthetic studies of some natural products in our laboratory, we became interested in the reactivity and regioselectivity of 1,3-dibromopropene (**4**) with carbonyl compounds in water.[4] Here, we wish to report that such a reaction mediated by indium in water generated bis-allylation products with both carbon-carbon bond formations occurring primarily on the same carbon, which effectively constitutes a gem-allyl dianion equivalent.[5]



4 **1** **(Eq. 2)**

Thus, when 1,3-dibromopropene was stirred with 3 equivalents of benzaldehyde and indium powder in water at room temperature for 16h, it resulted in a mixture of products (Scheme 1). Separation by column chromatography and spectroscopic analysis clearly indicate **6** as the major product, in which two benzaldehyde molecules are connected to the same carbon.[6] A more detailed characterization of minor products, as well as an investigation of factors affecting such a reactivity, were subsequently carried out. The results of these reactions are summarized and provided in Table I. Functional groups, such as hydroxyl, carboxylic acid, and nitrile, can tolerate the reaction conditions.

Scheme 1

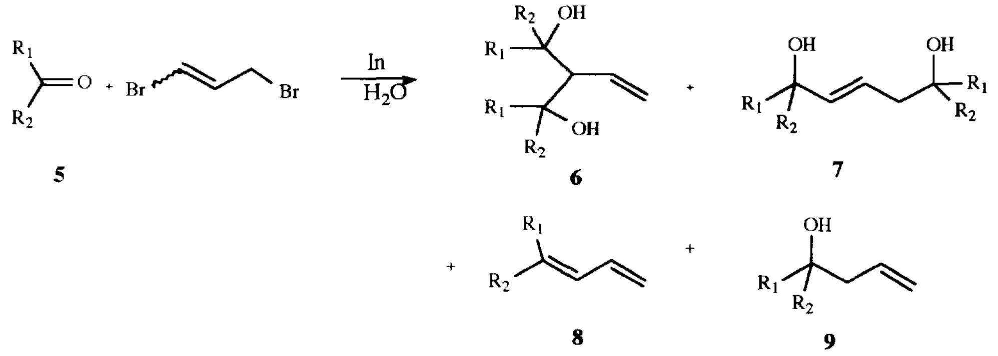


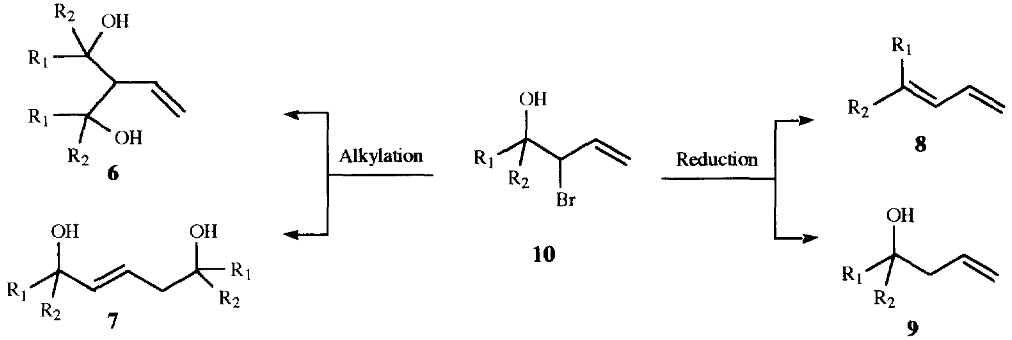
Table 1. Reaction of Aldehydes with Indium and 1,3-Dibromopropene in Aqueous Medium

Entry	Substrate	Temp(°C)/Time(h)	Product (isolated yield %)			
			6	**7**	**8**	**9**
1	PhCHO **5a**	r.t./16	54	8	7	22
2[a]	p-ClPhCHO **5b**	r.t./10	61	13	7	18
3	m-BrPhCHO **5c**	r.t./10	62	2	5	21
4[b]	p-NCPhCHO **5d**	r.t./11	62	10	3	23
5	p-HO$_2$CPhCHO **5e**	r.t./11	50	NI[c]	13	17
6	n-C$_6$H$_{13}$CHO **5f**	r.t./16	31	17	22	21
7	(CH$_3$)$_3$CCHO **5g**	r.t./17	0	11	NI[d]	10%
8	p-MePhCHO **5h**	r.t./16	23	2	32	32
9	p-HOCH$_2$PhCHO **5i**	r.t./12	11	NI[c]	29	51
10	p-MeOPhCHO **5j**	r.t./16	4	0	30	55

All reactions were carried out at 1 mmol scale based on 1,3-dibromopropene (aldehyde/1,3-dibromopropene/In powder = 3/1/3) in 8 ml water and under an atmosphere of air; a. 1 ml of THF was added; b. a 1:1 mixture of water/THF was used; c. not isolated; d. shown on TLC but not isolated due to its low boiling point.

In most cases during our investigation, the gem-bis-allylation products corresponding to the structure **6** were predominant. Compound **7**, a product corresponding to 1,3-bis-allylation, was generated in a small quantity in each case, as were dienes **8**[7] and simple allylation products **9**. These products may be formed from bromohydrin intermediate **10** *via* reductive elimination in the case of diene or direct bromine reduction in the case of homoallylic alcohol **9** (Scheme 2). As an indication of such a possibility, we have isolated compound **10**, when the reaction (using less indium) was interrupted after 30 min (for entry 1).

Scheme 2.



Aromatic aldehydes generally have a higher selectivity than aliphatic ones in product formations during the reaction. Unsubstituted and electron withdrawing group substituted benzaldehydes (Entries 1-5) gave mainly gem-bis-allylation products. Interestingly, for electron rich benzaldehydes (Entries 8-10), the formation of both gem- and 1,3-dialkylation products was dramatically decreased and the selectivity was reversed completely to give dienes and homoallylic alcohols. However, such a structural change does not affect the relative regio-selectivity of the bis-allylation reaction. These results indicate that the higher electron density of the aryl group somehow influenced and inhibited the mono-allylation product, preventing it from reacting further with another aldehyde. Alternatively, the electron donating group increased the rate of the reduction and elimination so that a second addition to a second equivalent of aldehyde is disfavored. Consequently, upon the reaction of indium with the mono-allylation product, the competing elimination and reduction processes were then predominant. Such a dramatic effect could be useful in understanding the mechanism of the aqueous Barbier-type reactions and in controlling the formation of either type of products through selective use of substituents.

A typical experimental procedure is as following: To a mixture of benzaldehyde (318 mg, 3 mmol) and 1,3-dibromopropene (200 mg, 1 mmol, mixture of *cis* and *trans*) in 8 ml water was added indium powder (345 mg, 3 mmol) in one portion. The reaction mixture was stoppered and stirred vigorously at room temperature for 16 h. The reaction was then stopped by the addition of 1 N HCl. The mixture was extracted with ether (4x10 ml). The combined organic phase was washed with brine, dried over magnesium sulfate and concentrated in vacuo. Flash column chromatography on silica gel through gradient-eluting with hexane/ethyl acetate (40:1 to 1:1) gave products **6a** (145 mg, 54%), **7a** (21.6 mg, 8%), **8a** (10.4 mg, 7%) and **9a** (30.8 mg, 20%).

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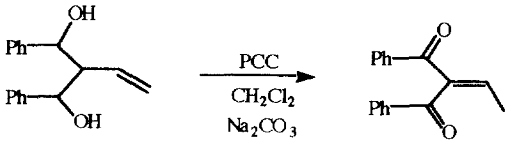
6. The structure was also confirmed chemically through PCC oxidation of the diol in which an ethylidene compound was generated.



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