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Selective Debromination of 1,1-Dibromoalkenes; A New Access to Di- or Trisubstituted Alkenes.

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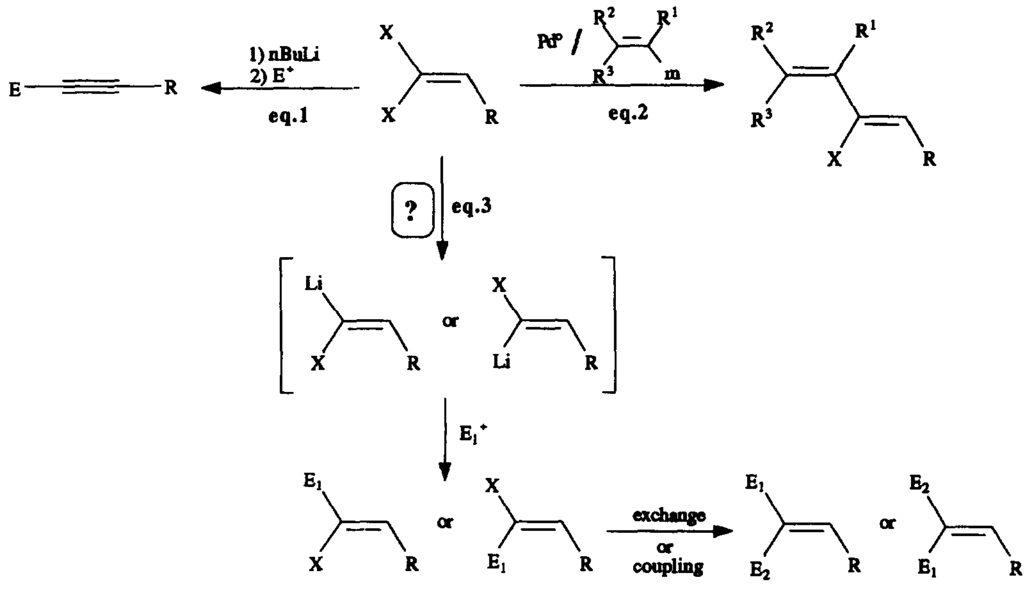
Abstract: *1,1-Dibromoalkenes were selectively debrominated by halogen-metal exchange. Depending on reagents and conditions, E-bromoalkenes can be obtained with very high stereoselectivity.*

1,1-Dihaloalkenes, easily obtained from aldehydes[1-3], are useful intermediates in organic synthesis. These dihalovinyl compounds are commonly used as acetylenic precursors (Scheme 1, eq.1).[1-2] More recently they have been used in Suzuki reactions, yielding (*1Z*)-2-halo-1,3-dienes with high stereoselectivity (Scheme 1, eq.2).[4-6]



Scheme 1: Chemistry of Dihalovinyl Compounds (E^+ = electrophile).

Dihalovinyl compounds have almost never been exploited using halogen-metal exchange[7]. Nevertheless such exchange should provide a functionnalized vinyl anion which could be trapped by various electrophiles yielding di- or trisubstituted haloalkenes (Scheme 1, eq.3, E_1^+= H or alkyl, carbonyl...). As a second halogen-metal exchange or alternatively a coupling reaction could be performed on the haloalkene so obtained (Scheme 1), this sequence might offer a new strategy for the synthesis of trisubstituted double bonds. Obviously, the development of this method as an useful tool in organic synthesis would rely on a stereoselective process.

In this communication, we present our preliminary investigations on 1,1-dibromoalkenes.[8] As expected, we found that dibromoalkenes quantitatively yielded monobromoalkenes when treated with one equivalent of organolithium followed by hydrolysis. A mixture of cis and trans bromoalkenes was obtained, the proportions of which can be significantly altered by the reaction conditions. We eventually found experimental conditions yielding *E*-bromoalkenes in a highly stereoselective manner. Our results are summarized in Table 1.

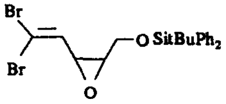
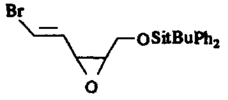
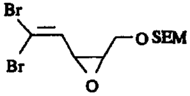
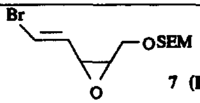
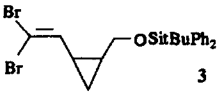
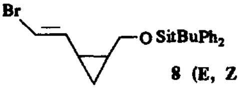
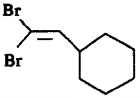
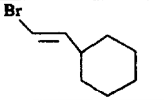
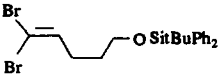
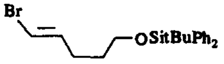
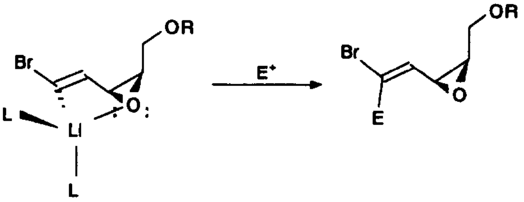
	dibromoalkene	reagent		T (°C)	yield[a]	E-Z[b]	products
1	 1	MeLi	THF	-105	96 %	100-0	 6 (E, Z)
2		MeLi	THF	-60	95 %	89-11	
3		MeLi	Et_2O	-105	5%[c]	50-50	
4		MeLi - LiBr	THF	-105	94 %	85-15	
5		MeLi	THF + HMPA	-105	98 %	85-15	
6		nBuLi	THF	-105	92%	80-20	
7		tBuLi	THF	-105	94%	85-15	
8		PhLi	THF	-105	96%	78-22	
9	 2	MeLi	THF	-90	98 %[d]	74-26	 7 (E, Z)
10		MeLi	THF	-60	95 %	70-30	
11	 3	MeLi	THF	-105	95 %	92-8	 8 (E, Z)
12		MeLi	THF	-90	96 %	79-21	
13	 4	MeLi	THF	-105	52 %[e]	98-2	 9 (E, Z)
14		MeLi	THF	-90	50 %[e]	95-5	
15	 5	MeLi	THF	-105	35%[f]	98-2	 10 (E, Z)
16		MeLi	THF	-90	25%[f]	95-5	

Table 1: a) yields refer to isolated products; b) determined by ^1H NMR of the crude mixture; c) >98% if calculated for a 95% conversion ; d) yield calculated for a 87% conversion; e) lower yield due to the volatility of the product.; f) the corresponding terminal alkyne was also isolated

Due to several ongoing programs related to the syntheses of natural products, we used the dibromovinylepoxide 1 as starting material for screening of reagents and conditions. Methyl lithium in THF at very low temperature proved to be the most selective reagent since only the *E*-bromovinyl epoxide 6 can be detected (entry 1). The nature of the organolithium species present in solution markedly influences the relative proportion of *Z* and *E* monobromoalkenes. With complex organolithium reagents, obtained by adding lithium bromide in the reaction mixture or more conveniently by using a commercial solution of an organolithium reagent complexed with lithium bromide, the selectivity decreased (entry 4 vs 1). Addition of HMPA to the reaction mixture also decreased the selectivity (entry 5 vs 1). n- or t-Butyl lithium, and phenyl lithium also showed a lower selectivity (entry 6, 7, 8 respectively). In each case, however, the *E* isomer was still predominant. The solvent is critical for the reaction to proceed. In THF the bromine-lithium exchange was very fast and quantitative, however ether slowed down the exchange to the extent that almost no reaction occurred (entry 3). Surprisingly in this case, almost no *Z*-*E* selectivity was observed

Temperature has only a minor influence on the *E*-*Z* ratio. Quenching experiments at various temperatures as well as TLC monitoring showed that a slight evolution of the cis-trans ratio occurred when the reaction temperature was higher than -105°, *e. g.* -60° (entries 2 vs 1).

The *E* stereoselectivity we obtained was naively interpretated as a chelation effect due to the presence of an electron lone pair on the oxygen atom of the oxirane ring. If initial complexation with this lone pair occurred, the favored isomer would be the chelated *E* vinyl lithium (Scheme 2) and therefore the major product after trapping would be the *E* bromoalkene. The presence of a chelating group inside the molecule would prevent chelation with the oxirane group and may therefore increase the amount of *Z* isomer. This was effectively observed when the SEM protected dibromovinyl epoxyalcohol 2 was treated with methyl lithium in THF, although the *E* isomer was still predominant (entries 9-10).



R = non-chelating protecting group
L = solvent or added ligand

Scheme 2

In order to check further this assumption, we prepared three dibromoalkenes where such chelation should be ineffective, two bearing a remote oxygenated group, 3 and 4, and one without any heteroatom 5. The results were quite surprising since in both cases, the halogen-metal exchange was still highly selective. With the cyclopropyl derivative 3, the *E*-*Z* ratio was better than 9 to 1 (entry 11). In this case however the reaction temperature significantly affected the isomer distribution (entry 12 vs 11). The linear analogue 4 proved to be even more selective since the *E* bromoalkene 8 was hardly exclusively obtained at very low temperature (entry

13)[9]. The cyclohexyl derivative **5** also provided the *E*-2'-bromovinyl cyclohexane **9** with very high stereoselectivity (entries 14 -15).

Obviously other factors than chelation intervene during halogen-metal exchange with 1,1-dibromoalkenes. Due to the complexity of the halogen-exchange mechanism[10], further experiments aimed to elucidate the observed *E* selectivity have to be done. Trapping experiments of the vinyl lithium generated through this method as well as synthetic applications are now under current investigations and will be reported in due course.

Typical procedure: To a solution of dibromovinyl derivative (1 mmol, 1 eq.) in dry THF (10 mL/mmol) under argon, was added at -105°C a commercial solution of organolithium (1 mmol, 1 eq.; Standardized before each use). After 5 mn at this temperature, the reaction mixture was quenched by methanol then by a saturated aqueous solution of ammonium chloride, then the resulting aqueous layer was extracted twice with diethylether. After drying and solvent evaporation, the product was chromatographied in the usual way.

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References

1) Synthesis of 1,1-dibromoalkenes:
Ramirez, F; Desai, N. B.; Mc Kelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745.
Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.
2) Synthesis of 1,1-dichloroalkenes:
Hosomi, A.; Inaba, M.; Sakurai, H. *Tetrahedron Lett.* **1983**, *24*, 4727.
Salmond, W. G.; Sobala, M. C.; Maisto, K. D. *Tetrahedron Lett.* **1977**, 1239.
Villieras, J.; Perriot, P.; Normant, J. F. *Synthesis* **1975**, 458.
3) Synthesis of 1,1-difluoroalkenes:
Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T. *Tetrahedron Lett.* **1990**, *31*, 5571.
4) Roush, W. R.; Moriarty, K. J.; Brown, B. B. *Tetrahedron Lett.* **1990**, *31*, 6509.
5) Minato, A.; Suzuki, K.; Tamao, K. *J. Am. Chem. Soc.* **1987**, *109*, 1257.
6) Minato, A. *J. Org. Chem.* **1991**, *56*, 4052.
7) To our knowledge, only one report mentioned the use of halogen-metal exchange for further elaboration of dibromovinyl derivatives. Although the underlying concept was similar, the context was however completely different since a single 1,1-dibromoalkene derived from lactaldehyde was used as an umpolung chiral form of a carbonyl group. Mahler, H.; Braun, M. *Chem. Ber.* **1991**, *124*, 1379; *Tetrahedron Lett.* **1987**, *28*, 5145.
8) Taken in part from the DEA report of D. Grandjean, 1987, Université de Reims-Champagne-Ardenne.
9) The unexpected direct formation of the terminal acetylene as the major product in this case (~60%) raises interesting mechanistic questions. Further works are now in progress in order to understand the reasons of this abnormal behavior.
10) See for example Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1989**, *111* , 3444, and references therein.

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