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Synthesis of stereo-defined 1,1,4,4-tetrahalo- and 1,1,4,4-mixed-tetrahalo-1,3-butadienes

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Abstract

Stereo-defined 1,1,4,4-tetrahalo- and 1,1,4,4-mixed-tetrahalo-1,3-butadienes were obtained in excellent yields via desilylation–halogenation of their corresponding 1,4-bis(trimethylsilyl)-1,4-dihalo-1,3-dienes, which could be readily prepared from the zirconocene-mediated high-yield and high-regioselective cyclo-dimerization of 1-trimethylsilyl-1-alkynes followed by halogenation. These poly-functionalized *gem*-dihalodienes are potentially useful building blocks.

Keywords: 1,1,4,4-Tetrahalo-1,3-butadienes; Desilylation–halogenation; *gem*-Dihaloalkenes; Zirconacyclopentadienes

Our results on the discovery and development of organo-bi-metallic reagents[1–3] have demonstrated that 1,4-dihalo-1,3-butadienes (Type I in Fig. 1) are of unique properties for organic synthesis because of the cooperative effect between the vinylhalide moiety and the butadienyl skeleton.[1–6] At the same time, *gem*-dihalovinyl systems (Type II in Fig. 1), as a class of important and versatile building blocks, have been applied widely in organic synthesis.[7–13] As our continued interest in the cooperative effect between the vinylhalide moiety and the butadienyl skeleton, we anticipated that a remarkable cooperative effect between the two *gem*-dihalovinyl moieties and the butadienyl skeleton in 1,1,4,4-tetrahalo- and 1,1,4,4-mixed-tetrahalo-butadienes (Type III in Fig. 1) may lead to unexpected interesting reaction patterns and synthetically useful methods. Although several cases of special types of tetrahalobutadienes have been reported in the literature,[14,15] we developed an alternative, versatile and convenient method for the preparation of 1,1,4,4-tetrahalo- and 1,1,4,4-mixed-tetrahalo-butadienes, via a conceptually new strategy shown in Scheme 1.

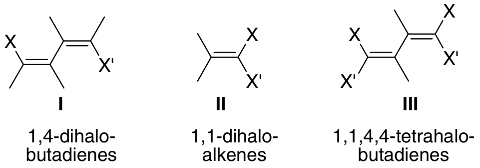

Fig. 1. Types of haloalkenes. X, X′ = I, Br, or Cl.

1-Trimethylsilyl-1-alkynes are well known to undergo zirconocene-mediated high-yield and high-regioselective cyclo-dimerization to afford zirconacyclopentadienes **3** (Scheme 1).[4,5,16] Halogenation of zirconacyclopentadienes **3** will give their corresponding 1,4-bis(trimethylsilyl)-1,4-dihalo-1,3-dienes **2** in excellent yields.[4,5,16] Then, desilylation–halogenation process should afford the expected 1,1,4,4-tetrahalo- and 1,1,4,4-mixed-tetrahalo-butadienes **1**. In this Letter, we report results obtained following the strategy given in Scheme 1.

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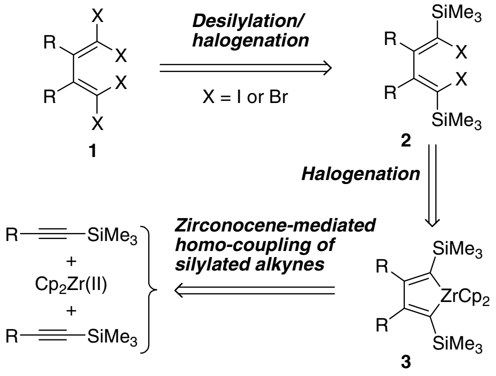
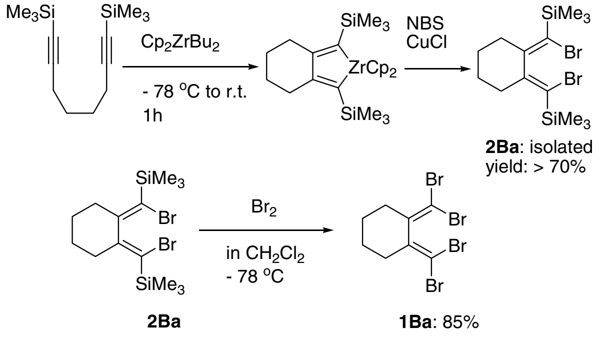


Scheme 1. New strategy for the synthesis of 1,1,4,4-tetrahalo-1,3-butadienes.

Firstly, we tried to prepare 1,1,4,4-tetrahalo-1,3-butadienes **1A**. Obviously, the type of 1,1,4,4-tetrahalides **1A** may be generated via desilylation/halogenation of their corresponding 1,4-bis(trimethylsilyl)-1,3-butadienes **2A**. Excellent procedures for the one-pot preparation of **2A** have been reported starting from 1-trimethylsilyl-1-alkynes and low valent zirconocene species (Negishi reagent, Cp_2ZrBu_2).[16] As shown in Scheme 2, a variety of **2A** could be isolated in high yields, generally in more than 90% isolated yields. After several trials, we found these compounds could be highly selectively desilylated and brominated using Br_2 at −78 °C in CH_2Cl_2 solvent. As expected, 1,1,4,4-tetrabromo-1,3-butadienes **1Aa** and **1Ab** were obtained in 92% and 94% isolated yields, respectively.[17] To the best of our knowledge, this method represents a novel methodology for these potentially useful polyhalo conjugated dienes. It should be pointed out that, when the substituents (R) at positions 2 and 3 were Ph groups, the desilylation/bromination process did not work well, affording product **1Ac** in much lower yield.

Similarly, a different type of tetrabromobutadienes, 1,2-bis(dibromomethylene)-cyclohexane **1Ba** was obtained in 85% isolated yield (Scheme 3).

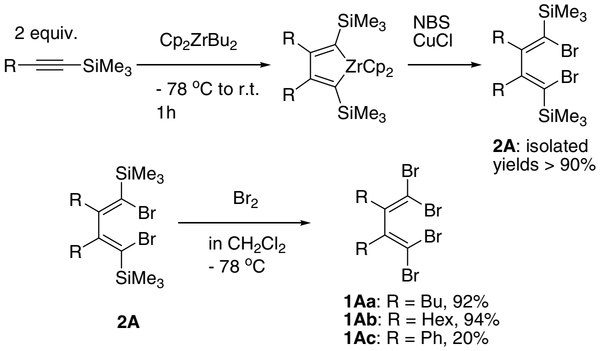
Zirconaindene intermediates **3C** could be readily generated via pair-selective cross-coupling of one molecule of benzene and one molecule of normal alkyne on low valent zirconocene species, as shown in Scheme 4.[18] Bromination of these intermediates using NBS in the presence of CuCl afforded the dibromo styrene derivatives **2C** in high isolated yields with perfect selectivity. Then, similar desilylation/bromination process gave *gem*-dibromovinyl-2-bromobenzene derivatives **1C**, a new type of polyhalides. Both **1Ca** and **1Cb** were obtained in excellent yields.



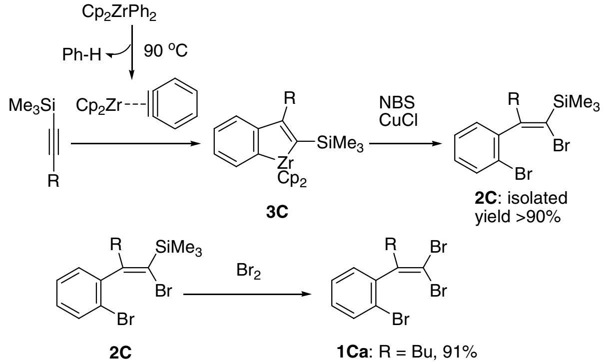
Scheme 3. Preparation of 1,2-bis(dibromomethylene)cyclohexane.

Unfortunately, several trials for desilylation/iodination and desilylation/chlorination under similar reaction conditions were ended in vein.

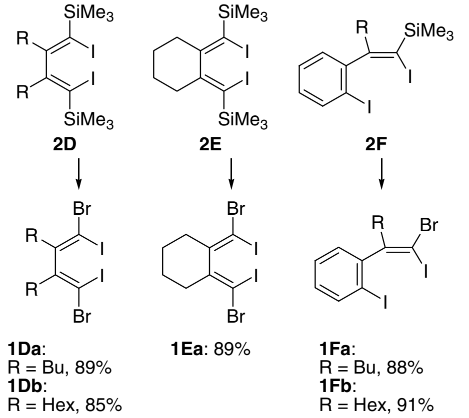
As discussed above, this strategy afforded polyhalides of types **1A**, **1B** and **1C**, all are brominated compounds. Since polyhalides with different halides should have more interesting and more complicated properties, and much more difficult to be prepared, particularly when regio- and stereo-selectivity are concerned. We then tried to synthesise polyhalides with different halides following the above simple strategy. To realize this synthesis, we firstly obtained diiodo compounds **2D**–**F** by iodination of their corresponding zirconacyclopentadienes.[4,5] Then, as given in Scheme 5, bromination of these diiodo compounds afforded their corresponding mixed polyhalo conjugated butadienes **1D**–**F**. (1*Z*,3*Z*)-1,4-Dibromo-1,4-diiodo-2,3-dibutyl-1,3-butadiene **1Da** and (1*Z*,3*Z*)-1,4-dibromo-1,4-diiodo-2,3-dihexyl-1,3-butadiene **1Db** were formed highly selectively in 89% and 85% isolated yields, respectively. (1*Z*,2*Z*)-1,2-bis(bromoiodomethylene)cyclohexane **1Ea** was obtained in 89% isolated yield. The structure of **1Ea**



Scheme 2. Preparation of 1,1,4,4-tetrabromo-2,3-disubstituted-1,3-butadiene derivatives.



Scheme 4. Preparation of *gem*-dibromovinyl-2-bromobenzene derivatives.



Scheme 5. Preparation of (1*Z*,3*Z*)-1,4-dibromo-1,4-diiodo-2,3-disubstituted-1,3-butadiene derivatives and 1-((*Z*)-2-bromo-2-iodovinyl)-2-iodobenzene derivatives.

was confirmed by single-crystal X-ray structural analysis (Fig. 2). Similarly, substituted 1-((*Z*)-2-bromo-2-iodovinyl)-2-iodobenzene derivatives **1Fa** and **1Fb** were obtained in 88% and 91% isolated yield, respectively.

More complicated polyhalides with different halides were also obtained following a similar procedure, with the main point of preparation of the key intermediates, the 1,4-mixed-dihalo-1,3-butadienes via step-by-step halogenation of zirconacyclopentadienes. The point to be successful was to use a less reactive halogenation reagent, for example, NBS as the first halogenation reagent, followed by a more reactive halogenation reagent, for example, I_2 and CuCl as promoter.[19] As given in Scheme 6, different types of polyhalides **1G**,**H** from the abovementioned **1D**–**F**, (*Z*)-1,1,4-tribromo-4-iodo-2,3-disubstituted-1,3-butadiene derivatives **1Ga**,**b** and (*Z*)-1-(bromoiodomethylene)-2-(dibromomethylene)-cyclohexane **1Ha** were generated in excellent yields. The structure of **1Ha** was confirmed by single-crystal X-ray structural analysis (Fig. 2).

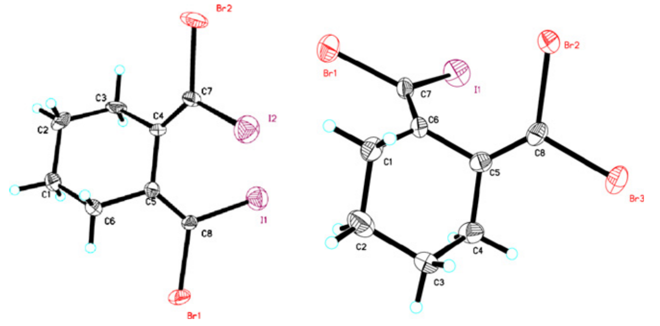
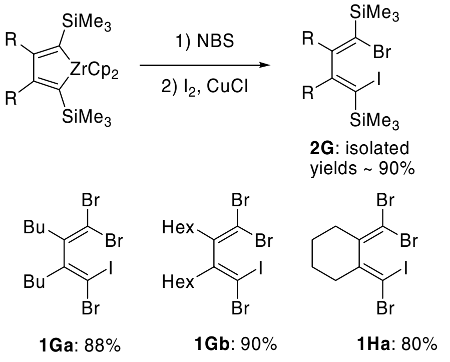


Fig. 2. X-ray structures of **1Ea** (left, CCDC 658988) and **1Ha** (right, CCDC 658989).



Scheme 6. Preparation of (*Z*)-1,1,4-tribromo-4-iodo-2,3-disubstituted-1,3-butadiene derivatives.

To achieve one-pot synthesis of 1,1,4,4-tetrabromo-1,3-dienes directly from 1-trimethylsilyl-1-alkynes via zirconacyclopentadienes **3** but without isolation of **2**, bromine was added directly to the reaction mixture containing **2Aa**. However, in THF, the desilylation/bromination process did not work, leaving **2Aa** unchanged although excess bromine in CCl_4 solution was used. In CH_2Cl_2, tribromides were obtained at −78 °C with high selectivity and at elevated temperature tetrabromides and unknown byproducts were both obtained.

In summary, we have developed a synthetically useful method for the preparation of interesting but otherwise unavailable polyhalo conjugated dienes, following a new strategy. Further synthetic application for organic synthesis is in progress in our laboratory.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.11.152.

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17. *General procedure for preparation of 1,1,4,4-tetrabromo-2,3-disubstituted-1,3-butadiene derivatives.* To a solution of 1,4-dibromo-1,4-bis(trimethylsilyl)-2,3-disubstituted-1,3-butadienes (1.0 mmol in 5.0 mL of CH_2Cl_2) was added dropwise 4.0 mmol Br_2 at −78 °C, and the mixture was stirred for 2 h at the same temperature. Then the resulting mixture was treated with 10.0 mL of 15% $NaHSO_3$ at −78 °C. The mixture was stirred at this temperature for 10 min and then warmed to room temperature. The mixture was maintained at ambient temperature for 30 min and was extracted with ether (3 × 10.0 mL). The combined organic layer was washed with saturated $NaHCO_3$, brine and water. After drying over $MgSO_4$ and evaporation of the solvent, column chromatography on silica gel with petroleum afforded the title product. *5,6-Bis(dibromomethylene)-decane* (**1Aa**): colorless liquid, isolated yield 92% (443 mg); ^{1}H NMR ($CDCl_3$) δ 0.90–0.98 (m, 6H, CH_3), 1.32–1.54 (m, 8H, CH_2), 2.09–2.18 (m, 2H, CH_2), 2.45–2.55 (m, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ 13.8 (2CH_3), 22.9 (2CH_2), 28.7 (2CH_2), 36.2 (2CH_2), 89.9 (2 quart C), 145.2 (2 quart C); HRMS calcd for $C_{12}H_{18}Br_4$ 477.8142, found 477.8133.
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