

SYNLETT Spotlight 242

1,2-Dibromoethane – A Versatile Reagent in Organic Synthesis

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Bhaskar Reddy Aluri was born in Hyderabad, India in 1979. He obtained his B.Sc. from Sri Krishna Devaraya University and his M.Sc. in Chemistry from the University of Hyderabad. After working for a short time in industry (Dr. Reddy's R & D division, Hyderabad) he joined the research group of Prof. Dr. J. Heinicke at the EMA University of Greifswald in 2005 and is currently working towards his Ph.D. His main interests lie in Organic Synthesis, Organometallic Chemistry, and Catalysis.

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Introduction

1,2-Dibromoethane (ethylene dibromide) is commonly used as an 'entrainment reagent' to chemically activate magnesium in Grignard reagents. It reacts with magnesium to expose a clean, reactive surface capable of converting otherwise unreactive halides into Grignard reagents.¹ It has many advantages over other entrainment agents. It reacts with magnesium to give $MgBr_2$ and ethylene as byproducts and hence does not introduce a second Grignard reagent to the system. 1,2-Dibromoethane is also a useful reagent for activating zinc.^{2,3} This reagent can be used as a source of electrophilic bromine for bromination of carbanions,⁴ and also acts as an alkylating agent with many enolates.⁵ 1,2-Dibromoethane is a precursor to numerous 1,2-disubstituted ethane derivatives, for example 1,2-ethanedithiol.⁶ In addition, it acts as a sacrificial reductant in the conversion of thiocarbonyl compounds to carbonyl compounds,⁷ and as an excellent oxidizer in domino carbopalladation–cyclization processes.⁸ It was used as a scavenger of lead antiknock agents in gasoline and as a soil fumigant for fumigation of grains and fruits until the early 1980s. It is a useful intermediate in the synthesis of dyes and pharmaceuticals.

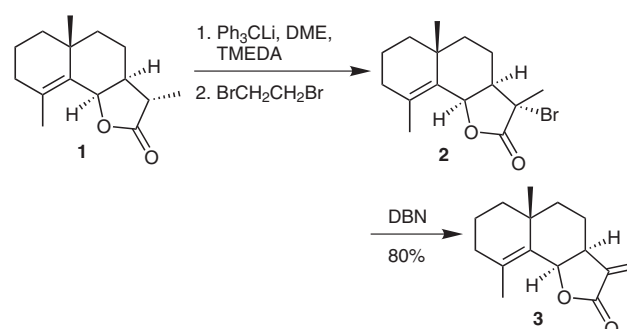
Preparation

1,2-Dibromoethane is commercially available, but can also be prepared by direct bromination of ethylene or by reacting hydrobromic acid with acetylene. Lesot et al. have reported that it can be prepared by bromination of 1,2-ethanediol in the presence of red phosphorus.⁹

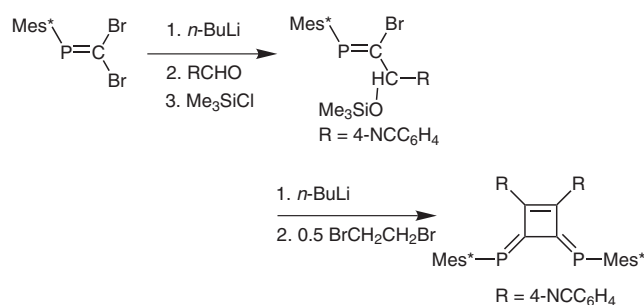
Properties

1,2-Dibromoethane is a colorless, heavy ($d = 2.18 \text{ g}\cdot\text{cm}^{-3}$) liquid with a mild, chloroform-like sweaty odor (mp $9\text{--}10\text{ }^\circ\text{C}$; bp $131.4\text{ }^\circ\text{C}$). It is miscible with all common organic solvents and itself a good solvent for resins, gums, and waxes. In the Cristol procedure for bromination of bridgehead acids, 1,2-dibromoethane is used as a solvent instead of CCl_4 to avoid the formation of chloride byproduct.¹⁰ Tests on animals indicated that over-exposure to this reagent may cause reproductive disorders. For humans it can cause damages to liver, kidneys, and lungs.

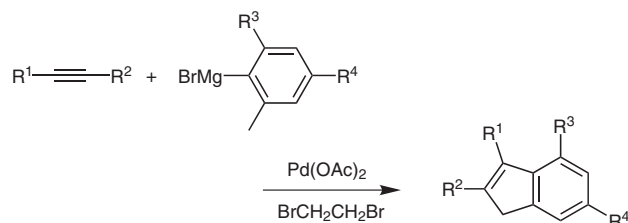
(A) In the synthesis of (–)-frullanolide **3**, a natural sesquiterpene, treatment of the enolate formed from lactone **1** with 1,2-dibromoethane afforded the α -bromolactone **2**. Dehydrobromination of **2** with excess 1,5-diazabicyclo[4.3.0]nonene-5 (DBN) afforded **3** in about 80% yield. This procedure is apparently the first example of the use of a *vic*-dihalide for formation of an α -haloketone.⁴



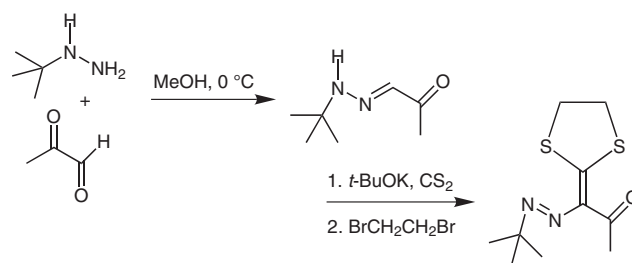
(B) Diphosphinidencyclobutenes (DPCBs) are rigid P2 ligand systems with strong π -accepting character that provide unique synthetic catalysts. To synthesize DPCBs with electron-withdrawing substituents, the classical route cannot be applied since a cyano group destabilizes the phosphallene and activates [3+2] dimerization. In the new approach 2-bromo-1-phosphapropene was treated subsequently with butyllithium and 1,2-dibromoethane to afford the desired cyano-substituted DPCB.¹¹



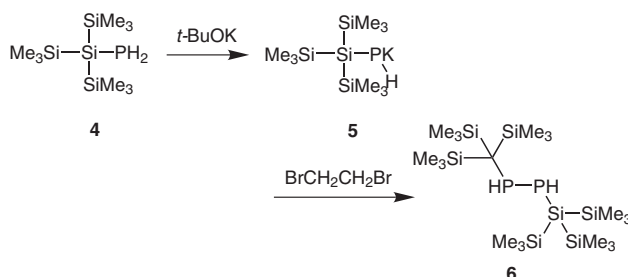
(C) For synthetic organic chemists, transition-metal-catalyzed tandem or domino reactions are very attractive because they allow the combination of two or more bond-forming reactions into one synthetic operation. In the Pd(OAc)₂-catalyzed domino carbopalladation–cyclization reaction of internal alkynes with hindered Grignard reagents, 1,2-dibromoethane acts as an excellent oxidant to give high yields of polysubstituted indenenes, which are structural constituents of metallocene-based catalysts for olefin polymerizations, of biologically active compounds, and of functional materials.⁸



(D) In the tandem reaction of pyruvaldehyde, *tert*-butylhydrazone, and CS₂, 1,2-dibromoethane acts as an alkylating agent to give the corresponding asymmetric azo-aliphatic compound.¹²



(E) 1,2-Dibromoethane is a useful reagent in the preparation of diphosphanes from PH compounds. An interesting example is the oxidative coupling of hypersilylphosphanides **5** to bulky P-secondary hypersilyldiphosphanes **6**, forming a mixture of *meso*- and *rac*-D,L-diastereomers. The hypersilylphosphanide **5** was synthesized by treatment of *t*-BuOK with hypersilylphosphane **4**. Interestingly, here *t*-BuOK will not cleave the P–Si bond but rather gives compound **5**, which is stable up to one week at room temperature.¹³



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