

A mild and selective dehydrohalogenating agent

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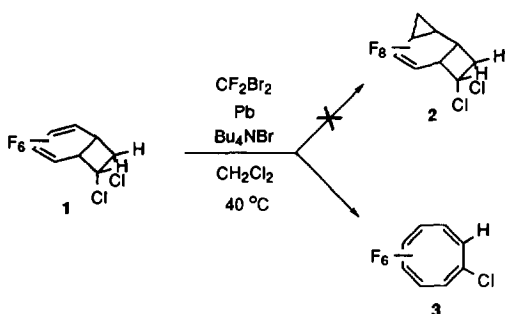
Abstract

A discriminating reagent has been discovered which effects E2 elimination of HX from relatively reactive substrates. Readily prepared from lead(II) oxide and lithium bromide hydrate, this compound is a hydrated lithium dibromoplumbite. © 1997 Elsevier Science S.A.

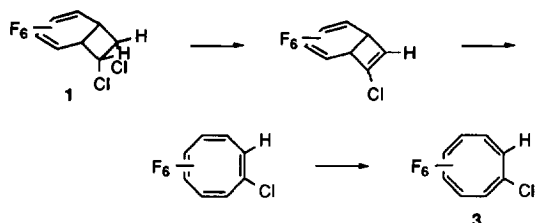
Keywords: Dehydrohalogenating agent; E2 elimination; Hydrated lithium dibromoplumbite

1. Results and discussion

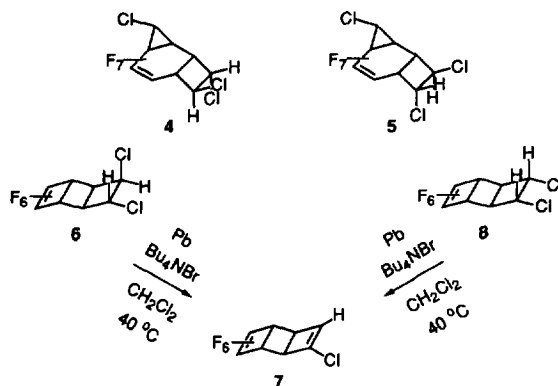
Attempts to add difluorocarbene to the bicyclic diene **1** by the method of Fritz and Kornumpf [1] gave a puzzling result. In this method, the carbene is generated from dibromodifluoromethane through the agency of lead powder and tetrabutylammonium bromide. No adduct **2** was obtained, presumably because of the electron deficiency of the substrate, but instead 1-chloro-2,3,4,5,6,7-hexafluorocyclooctatetraene (**3**) was slowly formed.



The generation of **3** required the dehydrochlorination of **1**, followed by electrocyclic ring opening and bond shift isomerization [2].



When compounds **4–6** [3] were subjected to the same reaction conditions, with the tetrahalomethane omitted, they underwent clean and complete dehydrochlorination. The reaction was particularly facile with the trans dichloride **6** [4], which gave diene **7** quantitatively at room temperature. Compound **8** [4], the cis stereoisomer of **6**, also underwent dehydrochlorination, but the reaction was about 50 times slower when both were carried out at 40 °C. (With certain substrates, reduction by lead(0) occurred to the exclusion of dehydrohalogenation. As an example, the stilbene dibromides suffered clean vicinal debromination instead of dehydrobromination when warmed with lead powder and tetrabutylammonium bromide in methylene chloride.) This marked contrast in reactivity is discussed below.



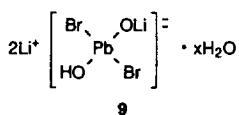
Substitution of lithium bromide hydrate (the bromide purchased from Aldrich was labeled $\text{LiBr} \cdot x\text{H}_2\text{O}$; we found our batch to contain 13 waters of hydration) in acetonitrile for tetrabutylammonium bromide in methylene chloride accelerated the dehydrochlorination of **6** by an order of magnitude at room temperature: the reaction was complete in 30 min.

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Ultrasound irradiation shortened the reaction time to 20 min. A finely divided white solid was deposited during the course of the reaction, and the same solid was observed when lead powder was stirred in acetonitrile containing lithium bromide hydrate in the absence of any substrate. This solid alone was found to dehydrochlorinate **6** quantitatively in acetonitrile at room temperature.

Clearly, the solid was behaving as a base, but the only base supposedly present was the gentle bromide ion; control experiments showed that lithium bromide alone was ineffective. Lead(0) cannot serve either, but it is known that lead powder undergoes surprisingly rapid oxidation to yellow lead(II) oxide when stirred in water which has not been deoxygenated [5]. Although our reactions were carried out under nitrogen, the solvent had not been degassed. It was therefore possible that the solid was a product of oxidation, a suggestion consistent with the fact that it was not formed in high yield. Indeed, when PbO was stirred in acetonitrile containing lithium bromide hydrate, the yellow color faded to white and the resulting solid was identical with that obtained starting with lead(0).

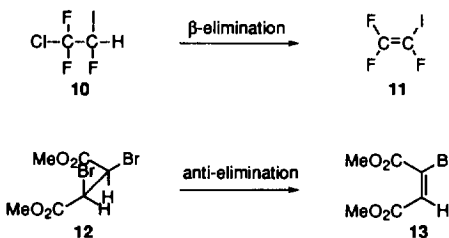
This air-sensitive substance was high melting (greater than 300 °C), insoluble in water and organic solvents, but soluble in aqueous acids and bases. When it was slurried in water, the supernatant became basic. Samples dissolved in 10% acetic acid were analyzed gravimetrically in our laboratory for bromine and lead (as AgBr and PbSO₄ respectively), and analyses for bromine and lithium were carried out by Galbraith Laboratories (Knoxville, TN, USA). All of the data are consistent with the formulation of the compound as a hydrated lithium dibromoplumbite **9** (its structure is probably similar to those of the plumbites K₂[PbCl₄] and K₂[Pb(HCO₂)₄] [6]).



The microanalytical results (the value given for bromine is the average of our result (34.20%) and Galbraith's (34.38%)) fit best for $x=2.5$ waters of hydration (calculated: Br, 34.30%; Li, 4.47%; Pb, 44.48%; found: Br, 34.29%; Li, 4.75%; Pb, 44.85%), but 2.0 is also possible (calculated: Br, 34.98%; Li, 4.56%; Pb, 45.35%). No acetonitrile was present in the solid.

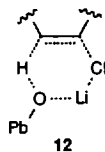
This reagent is extremely mild, eschewing such tempting substrates for elimination as cyclohexyl bromide and even tert-butyl bromide and the stilbene dibromides. Regarding its mechanism of action, slow reaction in acetonitrile with the chloriododifluorocarbon **10** yielded trifluoroiodoethylene (**11**), demonstrating that α -elimination of an excellent leaving group cannot compete with β -elimination of a poorer one. The lithium plumbite rapidly dehydrobrominated dimethyl-*meso*-2,3-dibromosuccinate (**12**), giving cleanly dimethyl- α -bromomaleate (**13**). The corresponding fumarate and the double elimination product dimethyl acetylenedicarboxylate

were not found. Thus the elimination took place exclusively in anti fashion as would be expected for an E2 reaction [7].



The fact that the dehydrochlorination of **6** (syn elimination) is rapid, whereas that of its stereoisomer **8** (anti elimination) is very sluggish deserves comment. Owing to the rigidity of the carbon skeleton, the transition state coplanarity required for E2 elimination cannot be achieved in **8** without considerable distortion. In contrast, the *trans* isomer **6** requires little or no conformational change for the four atoms involved in the elimination to become coplanar, a more important consideration than the inherent preference for anti-periplanar over synperiplanar transition state geometry [7].

Finally, the reactivity of the lithium plumbite is enhanced in the presence of lithium bromide hydrate or, to a lesser extent, lithium perchlorate. This finding suggests a role for the lithium ion in the elimination, probably assisting the departure of the halide ion. In the case of syn eliminations, such as those that occur with **4**, **5** and **6**, a cyclic transition state may be involved (**12**) [8].



Only substrates with moderately acidic hydrogens are sufficiently reactive to undergo dehydrohalogenation with the lithium plumbite reagent, but it is well suited for applications in which gentleness suffices and high selectivity is imperative.

2. Experimental details

¹⁹F NMR spectra were obtained at 56.2 MHz using a JEOL FX-60Q spectrometer or at 282.2 MHz with a Varian XL 300 instrument. Chemical shifts are reported on the Φ scale (parts per million from internal trichlorofluoromethane, upfield negative). ¹H NMR spectra were obtained at 300 MHz on a Varian XL 300 with tetramethylsilane as internal standard. Gas chromatographic analysis was performed on a Hewlett-Packard 5880A instrument equipped with a 12 m methylsilicone capillary column and flame ionization detector. GC/MS analyses were carried out on a Finnigan 4023 quadrupole mass spectrometer. Ultrasonic irradiation was performed in a Bronsicator Ultrasonic B-22-4 cleaning bath.

All solvents and reagents were of reagent grade. Dimethyl dibromosuccinate was prepared by Fisher esterification of

dibromosuccinic acid, which was purchased from Aldrich. Lead powder (200 mesh) was activated by washing with 1 N HCl (3×) and then with distilled water; it was dried in vacuo. The water content in $\text{LiBr} \cdot x\text{H}_2\text{O}$, obtained from Aldrich, was determined by heating samples with a flame to constant weight in a porcelain crucible and cooling in a desiccator; 13 waters of hydration were found.

2.1. Lithium dibromoplumbite hydrate

Into a 50 ml round-bottomed flask containing a stir bar was placed 3.2 g (10 mmol) of $\text{LiBr} \cdot 13\text{H}_2\text{O}$ and 35 ml of acetonitrile. To the resulting solution was added 1.0 g (4.5 mmol) of lead(II) oxide. The orange mixture was stirred at room temperature under nitrogen for 24 h. Filtration of the resulting white suspension was carried out in a Schlenk tube under positive nitrogen pressure, and the solid was washed quickly with acetonitrile (4×10 ml) and acetone (1×10 ml). The Schlenk tube was immediately evacuated to 0.05 Torr. When the solid was thoroughly dry, it was removed in a glove bag and stored under nitrogen (1.06 g, 68% yield).

The lead and bromine contents of the lithium dibromoplumbite hydrate were determined gravimetrically as follows. A sample (approximately 75 mg) of the solid was placed in a dry, nitrogen-purged, tared and stoppered 13 mm×100 mm test tube. The tube was weighed and placed open in an Abderhalden drying pistol to dry in vacuo (0.05 Torr) overnight at room temperature. (It was found that heating the sample led to inconsistent analytical results.) The pistol was filled with nitrogen and the tube was removed, quickly stoppered and weighed. The solid was dissolved in 10% acetic acid, and the resulting clear, colorless solution was treated with several drops of 1 M silver nitrate. Centrifugation was followed by further addition of silver nitrate until no more yellow silver bromide precipitated. All operations involving silver bromide were carried out in subdued light because of its light sensitivity. The clear supernatant was separated from the bromide, which was washed well with distilled water. After centrifugation, the water wash was combined with the original supernatant. Concentrated sulfuric acid was added to the aqueous solution, the mixture was centrifuged and more acid was added until no further precipitation of lead(II) sulfate occurred. The supernatant was removed and discarded. Both solids were washed with distilled water (3×3 ml) and acetone (3×3 ml). They were each dried in tared test tubes in a drying pistol at 56 °C, first at atmospheric pressure under nitrogen and then at 0.05 Torr for 24 h.

2.2. Dehydrochlorination of *trans*-7,8-dichloro-1,2,3,4,5,6-hexafluorotricyclo[4.2.0.0^{2,5}]octa-3,7-diene (6)

(A) Into a nitrogen-purged, 10 ml, pear-shaped flask was placed 720 mg (3.5 mmol) of lead powder and a solution of 96 mg (0.34 mmol) of **6** and 590 mg (1.8 mmol) of $\text{LiBr} \cdot 13\text{H}_2\text{O}$ in 4.5 ml of acetonitrile. The stoppered flask was half immersed in the ultrasound bath, where it was rocked

vigorously and sonicated for 20 min. Approximately 1 min after the start of the reaction, a finely divided white solid (the lithium dibromoplumbite) began to precipitate; its formation continued throughout the course of the reaction. During the reaction period, the bath temperature rose from 24 to 28 °C. ^{19}F NMR revealed 100% conversion to diene **7**, 7-chloro-1,2,3,4,5,6-hexafluorotricyclo[4.2.0.0^{2,5}]octa-3,7-diene. Its GC retention time at 35 °C was 1.72 min; that of **6** was 4.30 min. ^{19}F NMR of **7** (CH_2Cl_2): -119.5 (m, 2F, C₃, C₄), -177.2 (d, $J_{\text{FF}}=19$ Hz, 1F, C₁), -179.5 (dd, $J_{\text{HF}}=7$ Hz, $J_{\text{FF}}=19$ Hz, 1F, C₆), -187.3 (m, 2F, C₂, C₅). ^1H NMR (CD_3CN): δ 6.71 (d, $J=7$ Hz). GC/MS *m/e*: 248, 246 (ratio 1 : 3, M^+), 211 (base, $\text{M}^+ - \text{Cl}$), 192, 186, 161.

(B) Into a 10 ml round-bottomed flask containing a magnetic stir bar was placed 620 mg (1.9 mmol) of $\text{LiBr} \cdot 13\text{H}_2\text{O}$. To this was added a solution of 100 mg (0.35 mmol) of **6** and a small amount of hexafluorobenzene (as an internal integration standard) in 4 ml of acetonitrile. The mixture was stirred until the bromide dissolved, and then 750 mg (3.6 mmol) of lead powder was introduced. Stirring was continued for 1 h, and the very cloudy mixture which resulted contained the same white solid as described above. The yield of diene **7** was quantitative as judged by ^{19}F NMR integration.

(C) In a nitrogen-filled glove bag, 25 mg (0.054 mmol) of lithium bromoplumbite hydrate was placed in a 5 ml round-bottomed flask containing a stir bar. The flask was then charged with a solution of 22 mg (0.078 mmol) of **6** and 100 mg (0.31 mmol) of $\text{LiBr} \cdot 13\text{H}_2\text{O}$ in 2 ml of acetonitrile. The white slurry was stirred at room temperature under nitrogen for 0.5 h. ^{19}F NMR showed that conversion to diene **7** was 100%.

2.3. Dehydrobromination of dimethyl-meso-2,3-dibromosuccinate (12)

In a nitrogen-filled glove bag, 81.7 mg (0.175 mmol) of the bromoplumbite was placed in a 5 ml round-bottomed flask containing a stir bar, and a solution of 43 mg (0.14 mmol) of the ester in 2.25 ml of acetonitrile was added. The white suspension was stirred at room temperature under nitrogen for 30 min. ^1H NMR showed that the reaction was complete. The pale yellow reaction mixture was then centrifuged and the clear, colorless supernatant was stripped under reduced pressure to yield a white solid. Trituration with deuteriochloroform gave a solution which was analyzed by thin layer chromatography (TLC) (9 : 1 petroleum ether–ethyl acetate) and ^1H NMR. Dimethyl- α -bromomaleate (**13**) was the sole product. ^1H NMR: δ 3.76 (s, 3H), 3.89 (s, 3H), 6.49 (s, 1H). These chemical shifts are in excellent agreement with the literature values; the vinyl hydrogen of dimethyl- α -bromofumarate appears a full part per million to lower field [9].

Acknowledgements

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