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Reducing properties of 1,2-diaryl-1,2-disodiumethanes

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Abstract—1,2-Diphenyl- and 1-phenyl-2-(2-pyridyl)-1,2-disodiumethane efficiently dehalogenate *vic*-dibromoderivatives, affording the corresponding alkenes. The reaction proceeds rapidly, under mild conditions and is tolerant of a variety of functional groups (alcohol, carboxylic acid, ester and amide). This procedure was successfully extended to similar *vic*-disubstituted compounds.

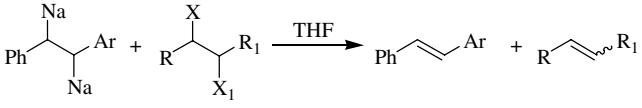
1. Introduction

Reduction of *vic*-dihalides to the corresponding alkenes by the action of mono-[1] or polycarbanions[2] is a known reaction, mainly investigated from a mechanistic point of view.

We recently reported a general procedure allowing the generation of 1,2-disodium-1,2-diarylethanes,[3,4] as well as their easy oxidation to the corresponding stilbenes by reaction with 1,2-dibromoethane,[3] probably occurring with contemporary formation of ethene.[2] Due to the synthetic significance of reductive dehalogenation procedures,[5] we investigated further on this reactivity, and wish to report some interesting preliminary results.

2. Results and discussion

Deep red solutions (0.1 M) of 1,2-diaryl-1,2-disodiumethanes **1a** and **1b** were obtained by the reaction of *trans*-stilbene or *trans*-stilbazole, respectively, with an excess of Na metal in dry THF, under Ar, immediately prior to use.[4,6] Solutions of **1** were drained from excess metal, and reductive eliminations were carried out by adding a solution of the *vic*-disubstituted compound **2** to a chilled solution of **1a** or **1b**, followed by stirring at the same temperature and aqueous workup (Scheme 1). Selected results are reported in Table 1.



1a, b **2a-i** **3a-i**

Scheme 1. 1,2-Diaryl-1,2-disodiumethanes-mediated reductive eliminations. **1a**, Ar = Ph; **1b**, Ar = 2-C_5H_4N; X and/or X_1 = Br, Cl, OCH_3; R, R_1, see text and Table 1.

Reaction of an *erythro*/*threo* = 9:1 diastereoisomeric mixture of 1,2-dibromo-1-(4-methoxyphenyl)propane,[7] **2a**, with 1.2 equiv of **1a** led, within 10 min at 0 °C, to the formation of *trans*-anetole, **3a**, inseparable from *trans*-stilbene, the product of oxidation of **1a** (Table 1, entry 1).

More efficiently, dehalogenation of **2a** was performed in the presence of 1.2 equiv of **1b**: after aqueous workup and acid washings (1 N HCl) to separate basic derivatives,[8] *trans*-anetole **3a** was recovered in almost quantitative yield (Table 1, entry 2).

This procedure was easily extended to the reductive dehalogenation of dibromocarboxylic acids. Indeed, by employing an excess of **1a**, quantitative dehalogenation of 10,11-dibromoundecanoic acid, **2b**, was obtained within 10 min at 0 °C (Table 1, entry 3). Application of this procedure to *threo*-13,14-dibromodocosanoic

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Table 1. 1,2-Diaryl-1,2-disodiumethanes-mediated reductive elimination reactions[a]

Entry	Dianion (equiv)	Substrate (R, R_1, X, X_1)	Product (R, R_1)	Yield (%)[b]
1	**1a** (1.2)	**2a** (4-$CH_3OC_6H_4$, CH_3, Br, Br) *erythro*/*threo* = 9:1	*trans*-**3a** (4-$CH_3OC_6H_4$, CH_3)	>95[c]
2	**1b** (1.2)	**2a** (4-$CH_3OC_6H_4$, CH_3, Br, Br) *erythro*/*threo* = 9:1	*trans*-**3a** (4-$CH_3OC_6H_4$, CH_3)	>90
3	**1a** (2.0)	**2b** (H, $(CH_2)_9COOH$, Br, Br)	**3b** (H, $(CH_2)_9COOH$)	80
4	**1b** (2.0)	*threo*-**2c** (C_8H_{17}, $(CH_2)_{11}COOH$, Br, Br)	**3c** (C_8H_{17}, $(CH_2)_{11}COOH$) *trans*/*cis* = 65:35[d]	>90
5	**1b** (2.0)	*erythro*-**2c** (C_8H_{17}, $(CH_2)_{11}COOH$, Br, Br)	**3c** (C_8H_{17}, $(CH_2)_{11}COOH$) *trans*/*cis* = >95: <5[d]	>90
6	**1a** (2.0)	**2d** (H, $(CH_2)_9OH$, Br, Br)	**3d** (H, $(CH_2)_9OH$)	70
7	**1b** (1.1)	**2e** (H, $(CH_2)_9OCOCH_3$, Br, Br)	**3e** (H, $(CH_2)_9OCOCH_3$)	82[e]
8	**1a** (1.1)	**2f** (see Scheme 2)	**3f** (see Scheme 2)	87
9	**1b** (1.3)	*erythro*-**2g** (Ph, Ph, Br, OCH_3)	*trans*-**3g** (Ph, Ph)	>90[f]
10	**1b** (1.1)	**2h** (H, $(CH_2)_{10}CH_3$, Cl, Cl)	**3h** (H, $(CH_2)_{10}CH_3$)	>95[c,f]

[a] All reactions were run at 0 °C during 10 min, unless otherwise indicated.
[b] Yields determined on isolated products, unless otherwise indicated.
[c] As determined by ^1H NMR of crude reaction mixture.
[d] As determined by GC–MS of the corresponding methyl esters (see text).
[e] Reaction run at −80 °C, under inverse addition conditions.
[f] Reaction time = 1 h.

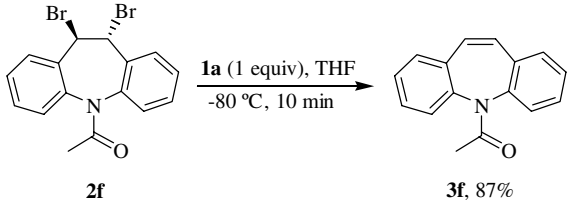
acid,[9] *threo*-**2c**, afforded the corresponding docos-13-enoic acid, **3c**, as a *trans*/*cis* = 65:35 diastereoisomeric mixture whilst, under identical reaction conditions, reductive dehalogenation of *erythro*-13,14-dibromodocosanoic acid,[9] *erythro*-**2c**, afforded almost pure *trans*-docos-13-enoic acid, **3c** (Table 1, entries 4 and 5). The ratio between the stereoisomers of **3c** was determined by esterification of crude reaction mixtures with diazomethane, followed by GC–MS analysis of the resulting products, whilst the stereochemistry of recovered **3c** was assigned by comparison with authentic samples of both stereoisomers.[9]

Under similar conditions, 10,11-dibromoundecan-1-ol, **2d**, was efficiently reduced to 10-undecen-1-ol, **3d**, by the reaction with 2 equiv of **1a** (Table 1, entry 6).

We next investigated the reaction of 10,11-dibromoundecyl acetate, **2e**, with dianion **1b**. Whilst a reaction run at 0 °C afforded a complex reaction mixture, a set of reactions run at −80 °C in the presence of variable amounts of **1b** (1–2 equiv), led to the recovery of reaction mixtures containing, besides 10-undecenyl acetate, **3e**, variable amounts of starting material and 10-undecen-1-ol, **3d**. We rationalized this behavior by assuming that **1b** acts both as a reducing agent, leading to the formation of dehalogenated products, as well as a nucleophile, leading to cleavage of the ester bond and, eventually, to the formation of alcohol **3d**. However, under inverse addition conditions, that is, by dropwise adding 1.1 equiv of **1b** to a chilled solution of ester **2e**, it was possible to recover the desired unsaturated ester **3e** in 82% yield (Table 1, entry 7).[10]

It is worth noting that a less electrophilic amide did not pose similar problems: indeed, addition of amide **2f**[11] to a chilled THF solution of 1.1 equiv of **1a** afforded the desired dehalogenated product, **3f**, in satisfactory yield (Table 1, entry 8 and Scheme 2).

Our procedure was successfully extended to similar *vic*-disubstituted compounds. Indeed, reduction of *erythro*-1-bromo-2-methoxy-1,2-diphenylethane,[12] **2g**, with an excess of **1b** at 0 °C during 1 h, efficiently afforded *trans*-stilbene, **3g** (Table 1, entry 9); under similar conditions, reaction of 1,2-dichlorododecane, **2h**, with a slight excess of **1a**, allowed the recovery of 1-dodecene, **3h**, in satisfactory yield (Table 1, entry 10).



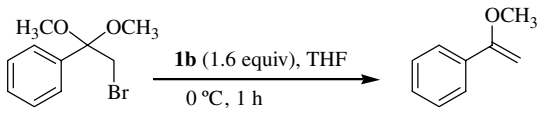
2f **3f**, 87%

Scheme 2. Reductive dehalogenation of amide **2f**.

Finally, we investigated the reductive elimination of 1-phenyl-1,1-dimethoxy-2-bromoethane, **2i**, and found that its reduction with 1.6 equiv of **1b** afforded 1-phenyl-1-methoxyethene, **3i**, in satisfactory yield (Scheme 3).

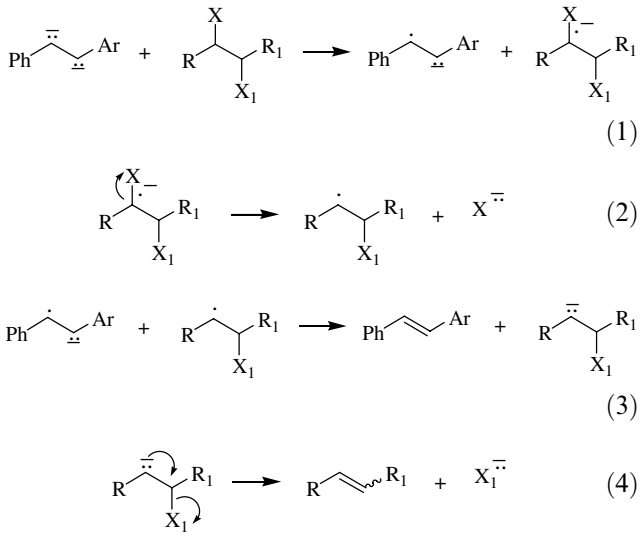
From a mechanistic point of view, the described reductive elimination reaction can be considered to proceed via a 'single electron' reaction pathway,[13] as described in Eqs. 1–4.

A first SET from the dianion to the *vic*-disubstituted substrate generates two different radical anions (Eq. 1); the halide-substituted radical anion undergoes an halide–carbon bond cleavage, thus affording a halide anion and a radical (Eq. 2); a second SET, from the 1,2-diaryl radical anion to the radical, afforded the 1,2-diarylethene and a β-substituted carbanion (Eq. 3); in the last step, the β-substituted carbanion is transformed into the corresponding alkene (Eq. 4).



2i **3i**, 70%

Scheme 3. Reductive elimination of **2i**.



In agreement with this hypothesis, with suitable substrates our reductive elimination procedure occurs with preferential or exclusive formation of *trans*-alkenes (Table 1, entries 1, 2, 4, 5, 8 and 9), as in the case of Na naphthalenide-promoted reductive debrominations.[5k]

In summary, our results clearly show that 1,2-diaryl-1,2-disodiumethanes efficiently promote the reductive elimination of *vic*-dibromides and related *vic*-disubstituted derivatives. Interestingly, our procedure is tolerant of a variety of functional groups (Table 1, entries 3–8 and Scheme 2). Further work is in progress to extend the scope of this reaction.

3. General experimental procedure

Deep red solutions (0.1 M) of **1a** or **1b** were prepared by the reaction of freshly cut Na metal with stilbene or azastilbene, respectively, in dry THF, as reported in Ref. 4. These solutions were prepared, and drained from excess metal under an atmosphere of pure argon, immediately before use. The preparation of starting materials was realized with standard procedures. THF was distilled from Na/K alloy under N_2 immediately prior to use.

4. Typical reductive elimination procedure

To 10 mL of 0.1 M solution of **1a** or **1b** (1 mmol), chilled at 0 °C, was added a solution of the appropriate *vic*-disubstituted compound **2** (0.8–0.5 mmol) dissolved in 3 mL of dry THF. After stirring for 10 min (except when otherwise indicated), the mixture was quenched by slow dropwise addition of H_2O (15 mL), the cold bath removed, and the resulting mixture extracted with Et_2O (3×10 mL). The organic phase was washed with brine (10 mL) then, in case of reactions with **1b**, with 1 N HCl (3×10 mL), dried (Na_2SO_4) and the solvent evaporated.

Crude products from reactions run in the presence of **1a** were purified by flash chromatography (petroleum ether/AcOEt), whilst crude products from reactions run in the presence of **1b** were usually >90% pure (^{1}H NMR and GC–MS).

Although the synthesis of compound **3i** was run in the presence of **1b**, the reaction product, which is acid sensitive, was purified by flash chromatography (petroleum ether/AcOEt/Et_3N).

All compounds gave analytical and spectral (^{1}H and ^{13}C NMR, IR) data in agreement with the assigned structures and available literature data; the stereochemistry of starting materials and reaction products was assigned by comparison with commercially available samples (*trans*-**3a**, *cis*-**3c**, *trans*-**3g**), or with literature data (**2a**,[7] *threo*-**2c**,[9] *erythro*-**2c**,[9] **2f**,[11] *erythro*-**2g**,[12] *trans*-**3c**[9]).

Acknowledgements

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