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# TRIMETHYLENEMETHANE DIANION EQUIVALENT IN AQUEOUS MEDIUM[1]

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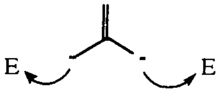
**Summary:** *Via an indium mediated Barbier-type reaction in aqueous medium, carbonyl compounds react with a trimethylenemethane dianion equivalent to give the corresponding diols.*

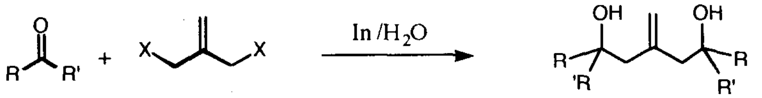
Trimethylenemethane dianion **1** is a valuable reagent for organic synthesis.[2] By reacting with two nucleophiles, such as alkyl halides,[3] carbonyl compounds,[4] epoxides and nitriles,[5] the corresponding double-alkylation products are generated. Normally, the dianion is generated by either double deprotonation of isobutene[3-5] or a halogen-lithium exchange reaction at low temperature.[2c,4b] In connection with our efforts to develop environmentally benign procedures for organic synthesis, we are interested in generating a trimethylenemethane dianion equivalent in water. In this report, such a trimethylenemethane dianion equivalent reacts with two carbonyl compounds sequentially *via* an indium mediated[6] Barbier-type reaction in aqueous medium,[7] generating the corresponding diols.



**1**

Stirring benzaldehyde with 2-chloromethyl-3-chloro-1-propene and indium in a 1:1 mixture of water/methanol for 1 h at room temperature gave 18% isolated yield of a diol as a 1:1 mixture of diastereomers. Replacing 2-chloromethyl-3-chloro-1-propene by 2-bromomethyl-3-bromo-1-propene[8] dramatically increased the rate of the reaction. Reaction of benzaldehyde and indium with the bromo compound in a 1:1 mixture of methanol/0.1N HCl gave 75% of isolated yield of the same product after 30 min, whereas the same reaction in water alone led to a 21% yield of the product within 10 min.

The efficiency of this novel trimethylenemethane dianion equivalent led us to investigate a range of carbonyl compounds that serve as the electrophiles. The results are summarized in table 1. An aliphatic aldehyde reacted as effectively as an aromatic aldehyde did (entry 5). Reaction of the dianion equivalent with cyclohexanone gave a relatively lower yield of the product (entry 6). A noticeable result is the reaction of the dianion equivalent with m-chlorobenzaldehyde (entry 4). The reaction occurs smoothly generating the diol without affect the chloro group. The traditional approaches by either lithiation of isobutene or 2-chloromethyl-3-chloro-1-propene would have great difficulty to prevent the halogen-lithium exchange reaction of the aromatic chloride.[3-5] The current method successfully avoided such a competing side-reaction. Practical application of this convenient trimethylenemethane dianion equivalent can be expected.

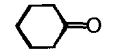


**2** **3** **4**

(1)

A typical experimental procedure follows: To a stirring mixture of p-methylbenzaldehyde (360 mg, 3 mmol) and 2-bromomethyl-3-bromo-1-propene (212 mg, 1 mmol) in 5 ml of methanol/ 0.1 N HCl (1: 4) was added indium powder (230 mg, 2 mmol). After stirring for 1 h at room temperature, 1 N HCl was added. The reaction mixture was extracted with ether (4 x). The combined organic fractions were washed with brine, dried over sodium sulfate and concentrated. The diol product (201 mg, 68%) was isolated by column chromatography on silica gel (hexane/ethyl acetate, 4:1).

**Table 1. Reaction of the Trimethylenemethane Dianion Equivalent with Carbonyl Compounds**

| Entry | R- | R'- | X- | Time | Solvent[a] | Yield(isolated)[c] |
|---|---|---|---|---|---|---|
| 1 | Ph- | **H-** | **Br-** | 0.5h | 1/1 | 75 |
| 2 | Ph- | **H-** | **Cl-** | 1h | 1/1[b] | 18 |
| 3 | p-MePh- | **H-** | **Br-** | 1h | 4/1 | 68 |
| 4 | 3-ClPh- | **H-** | **Br-** | 1h | 4/1 | 53 |
| 5 | $CH_3CH_2$- | **H-** | **Br-** | 3h | 4/1 | 61 |
| 6 |  |  | **Br-** | 3h | 4/1 | 19 |

[a] The ratio is methanol/0.1 N HCl (aqueous solution); [b] methanol/water; [c] All the reactions generate a 1:1 mixture of diastereomers, except for entry 6.

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