

# SYNLETT Spotlight

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

## Copper(II) Bromide

Compiled by Anton Makarov

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Dedicated to the memory of my father, Sergey Makarov, M.D.

*Aliis inserviando ipse consumor*



### Introduction

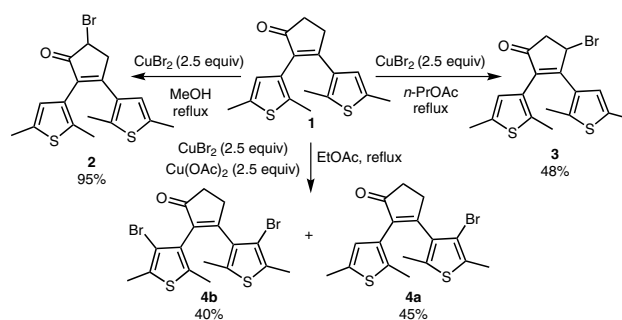
Copper(II) bromide is a black crystalline powder with a melting point of 498 °C and a boiling point of 900 °C. It is soluble in water, alcohol and acetone; however, it is insoluble in benzene and ether. Copper(II) bromide can be obtained by the reaction of copper(II) oxide with hydro-

bromic acid or by the reaction of metallic copper with bromine.

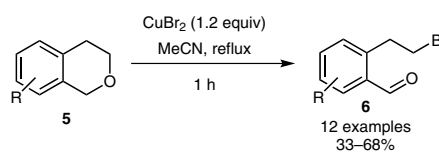
Copper(II) bromide is a powerful brominating agent.<sup>1</sup> It is also used as a catalyst in many organic reactions, including alkylation,<sup>2</sup> amination,<sup>3</sup> oxidation,<sup>4</sup> multi-component reactions,<sup>5</sup> and for the synthesis of ethers<sup>6</sup> or esters.<sup>7</sup>

### Abstracts

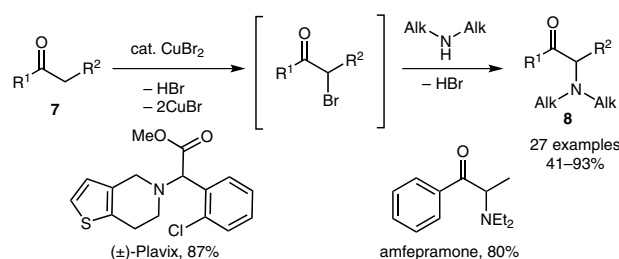
(A) Shirinian and co-workers developed a regio- and chemoselective method for the bromination of 2,3-diarylcyclopent-2-en-1-ones with copper(II) bromide. Different brominated products can be obtained depending on the reaction conditions utilized in case of 2,3-bis(2,5-dimethylthiophen-3-yl)cyclopent-2-enone (**1**). The formation of **2** and **3** is suggested to proceed via the reaction of in situ generated enolates with cationic Cu–Br species while **4a** and **4b** are formed by S<sub>E</sub>Ar.<sup>8</sup>



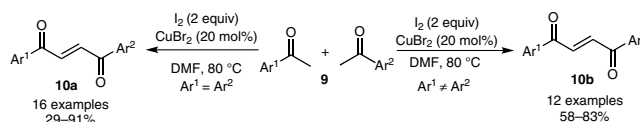
(B) Zhou et al. described a mild and efficient method for the oxidation–bromination of isochromans **5** to afford the corresponding 2-(2-bromoethyl)benzaldehydes **6** in one step with an excess of copper(II) bromide.<sup>9</sup>



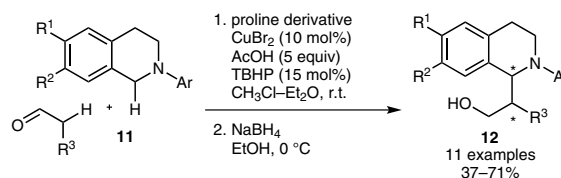
(C) Recently, a green generic approach to complex  $\alpha$ -amino carbonyls **8** via the CuBr<sub>2</sub>-catalyzed coupling of carbonyls **7** and diverse secondary amines was described. The transformation is proposed to proceed via an  $\alpha$ -bromo carbonyl species. The practical utility of this transformation was highlighted by one-step syntheses of two high-profile pharmaceutical agents, Plavix and amfepramone.<sup>10</sup>



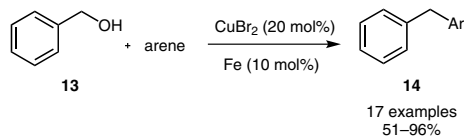
(D) Wang and co-workers reported a simple protocol for the synthesis of symmetric and unsymmetric (*E*)-2-ene-1,4-diones **10** by the reaction of acetophenones **9** with molecular iodine. The use of copper(II) bromide dramatically improved the yields of the desired products.<sup>11</sup>



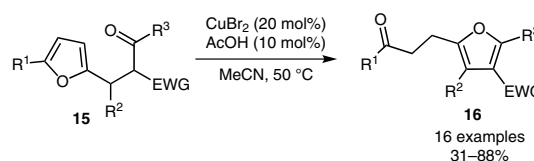
(E) Chi and co-workers reported a CuBr<sub>2</sub>-catalyzed enantioselective oxidative cross-coupling reaction of tertiary amines **11** with aldehydes in the presence of a proline derivative as a chiral catalyst. The unstable aminoaldehydes were reduced in situ by sodium borohydride to afford  $\gamma$ -amino alcohols **12** with good enantioselectivity.<sup>12</sup>



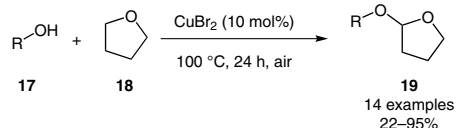
(F) An efficient and inexpensive Fe/CuBr<sub>2</sub>-catalyzed benzylation of arenes and thiophenes under mild conditions was described. The method provides diarylmethanes **13** with good to excellent yields using the readily available benzyl alcohol **14** as a benzylating agent.<sup>13</sup>



(G) Yin and co-workers reported a mild method for the preparation of polysubstituted furans **16** via copper(II) bromide catalyzed rearrangement of furans **15**. This protocol provides an efficient access to tetrasubstituted furans, which are usually synthesized through multi-step procedures utilizing harsher reaction conditions.<sup>14</sup>



(H) Deng and co-workers developed a method for copper(II) bromide promoted tetrahydrofuranation of alcohols **17** with unsubstituted tetrahydrofuran **18**. The protocol might be used for the protection of hydroxyl groups.<sup>15</sup>



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