

# SYNLETT Spotlight 207

## Ruthenium(III) Chloride ( $\text{RuCl}_3$ )

Compiled by Jason T. Lowe



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

Jason completed his undergraduate degree (1998) in chemistry and geology at the University of Rhode Island. He would stay to finish a M.S. degree in organic chemistry (2001) under the tutelage of Prof. William Rosen. After a brief period of working as a process chemist for Rhodes Technologies (subsidiary of Purdue Pharma) he joined Prof. James S. Panek's lab at Boston University. His current research interests include developing organosilane-based methodologies for application in natural product synthesis. Jason has recently received an ACS Division of Organic Chemistry Fellowship (2006) and is the recipient of a Merck Graduate Fellowship (2007).

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### Introduction

Ruthenium(III) chloride and its hydrate ( $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$ ) are well-known catalysts for the oxidation of functional groups in organic synthesis. Some of these transformations include: alkenes to diols<sup>1</sup> and  $\alpha$ -hydroxyketones,<sup>2</sup> sulfides to sulfones,<sup>3</sup> as well as alkynes,<sup>4</sup> alcohols<sup>5</sup> and aryl groups<sup>6</sup> to their corresponding carboxylic acids. The titled catalyst has also been used for the desymmetrization of aryl and benzyl diselenides,<sup>7</sup> aldol condensation,<sup>8</sup> formation of  $\alpha$ -aminonitriles (Strecker reaction),<sup>9</sup> acylation,<sup>10</sup> acetal formation,<sup>11</sup> aryl<sup>12</sup> or azide<sup>13</sup> reductions, conjugate addition reactions<sup>14</sup> and C–C bond formations.<sup>15</sup>

Apart from the use of ruthenium(III) chloride in functional group manipulation, recent work has used  $\text{RuCl}_3$  in the formation of polypyridine complexes, suggesting that this

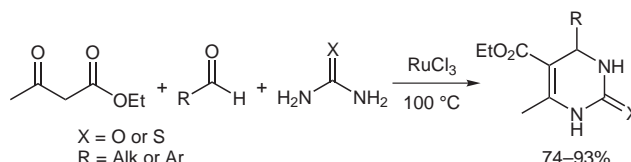
reagent may soon experience a wider application in metallopolymer and molecular-device synthesis.<sup>16</sup>

Ruthenium(III) chloride is also a critical ingredient for preparing a number of ruthenium-based catalysts, including Grubbs' catalysts (widely applied in metathesis reactions)<sup>17</sup> and ruthenium–phosphine complexes capable of selective reductions.<sup>18</sup>

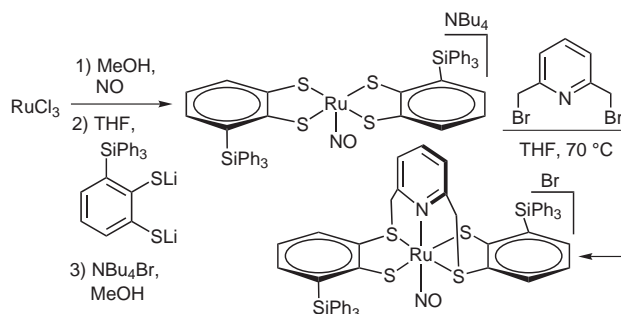
Both anhydrous and hydrated forms are commercially available as solids. Alternatively, the solids may be prepared by heating powdered ruthenium metal to temperatures greater than 700 °C in the presence of chlorine gas; on cooling, dark brown to black crystals may form.<sup>19</sup> Although their hygroscopic nature mandates storage in desiccated environments, no additional precautions are required for safe handling.

### Abstract

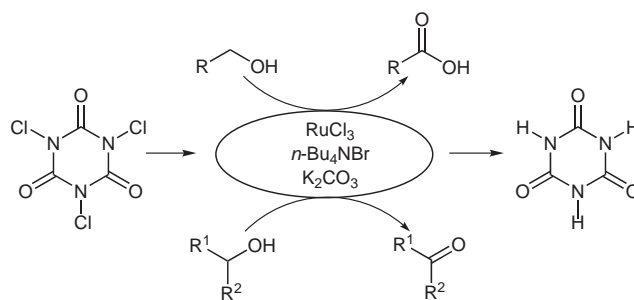
(A) A solvent-free Biginelli reaction utilizing  $\text{RuCl}_3$  was recently reported.<sup>20</sup> The reaction was shown to be wide in scope covering aromatic, conjugated and aliphatic aldehydes to form either the pyrimidin-2(1*H*)-one or thione heterocycles. Acetonitrile was identified as an appropriate solvent if one was required. Yields were found to be very good for all reported reactions.



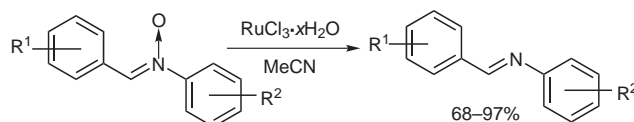
(B) A reaction using  $\text{RuCl}_3$  to form a nitric oxide bound ruthenium dithiolate bridge complex was recently reported.<sup>21</sup> The ability of ruthenium to reversibly complex nitric oxide has attracted attention for possible use in a number of biological applications.



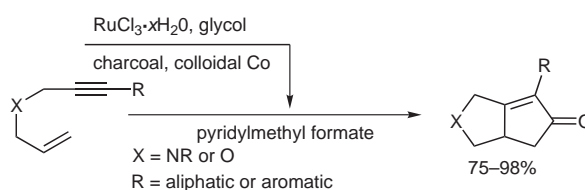
(C) Generation of  $\text{RuO}_4$  from  $\text{RuCl}_3$  is well documented for the formation of carboxylic acids and ketones from primary and secondary alcohols. Typical conditions employ  $\text{NaIO}_4$  as a stoichiometric oxidant in a biphasic solvent system ( $\text{CCl}_4/\text{MeCN}/\text{H}_2\text{O}$ ). A recent paper by Ikunaka showcases a much more environmentally benign approach using trichloroisocyanuric acid as a stoichiometric oxidant,  $n\text{-Bu}_4\text{NBr}$  as phase transfer catalyst and  $\text{MeCN}/\text{H}_2\text{O}$  or  $\text{EtOAc}/\text{H}_2\text{O}$  as solvent system.<sup>22</sup> Yields are comparable to traditional conditions using  $\text{NaIO}_4$ .



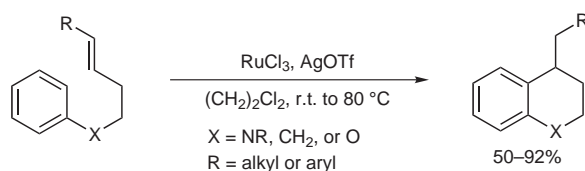
(D) Deoxygenation of substituted aromatic  $N$ -oxides using stoichiometric  $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$  has been reported.<sup>23</sup> The methodology was also extended to incorporate azoxybenzenes and  $N$ -heteroarene oxides giving deoxygenated products in good yields.



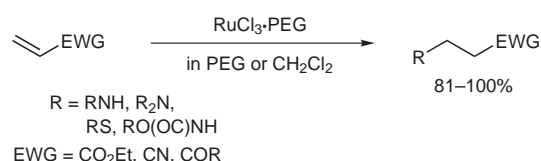
(E) Heterobimetallic  $\text{Ru-Co}$  nanoparticles, derived from ruthenium chloride and colloidal cobalt, were used in a Pauson–Khand-type reaction to access a number of bicyclic systems.<sup>24</sup> The reaction also employed pyridylmethyl formate as a chemical alternative to carbon monoxide. High yields were observed for both intra- and intermolecular systems.



(F)  $\text{RuCl}_3$  was found to effect the formation of arene heterocycles and carbocycles.<sup>25</sup> The reaction requires  $\text{AgOTf}$ , presumably to activate the ruthenium in situ. Numerous catalytic systems, both  $\text{Ru}$ - and non- $\text{Ru}$ -based, were explored with little success.



(G) Michael addition of primary and secondary amines, thiols and carbamates to  $\alpha,\beta$ -unsaturated esters, nitriles and ketones using catalytic  $\text{RuCl}_3\text{-PEG}$  (polyethylene glycol) was recently reported.<sup>14</sup> High yields were observed for all systems examined. The catalyst was recycled with little decrease in product yield.



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