# Novel Catalysts for the Overman Rearrangement

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**Abstract:** PtCl<sub>2</sub>, PtCl<sub>4</sub>, AuCl, and AuCl<sub>3</sub> were found to be efficient catalysts for the Overman rearrangement of *O*-allyltrichloroacetimidates to *N*-allyltrichloroacetamides.

Key words: amines, amides, rearrangement, catalysis, Lewis acids

The aza-Claisen rearrangement of O-allyltrichloroacetimidates to N-allyltrichloroacetamides was first demonstrated by Overman and since then it has found widespread application as a C-N bond forming reaction.<sup>1</sup> Trichloroacetimidates are readily available from allylic alcohols and the trichloroacetyl group in the products can be relatively easily cleaved rendering the Overman rearrangement a method of choice for the synthesis of primary allylamines.<sup>1,2</sup> The rearrangement can be performed thermally at elevated temperatures (typically 110-140 °C) or can be catalyzed by Hg(II) and Pd(II) salts under very mild reaction conditions.<sup>1,3</sup> The catalytic approach offers additional opportunities - chelation controlled diastereoselectivity has been reported for the Pd(II)-catalyzed rearrangement providing protected *anti*-1,2-amino-alcohols<sup>4</sup> and 1,2-diamines.<sup>5</sup> Moreover, the first chiral cobalt oxazoline palladacycle catalyst has been recently developed for the enantioselective rearrangement of trichloroacetimidates.1d,e

To the best of our knowledge Hg(II) and Pd(II) salts are the only efficient catalysts reported to date for Overman and related imidate rearrangements,<sup>3a,6</sup> although the potential utility of other metals has been mentioned.<sup>3b</sup> We believed that broadening the scope of catalysts for the Overman rearrangement would offer new perspectives for this useful transformation, in particular with respect to stereochemical aspects.

The search for new catalysts began with the screening of metal salts and alkoxides using trichloroacetimidate **1a** ( $R^1 = Me$ ,  $R^2 = H$ ) as a model substrate in  $CH_2Cl_2$ 

(Scheme 1). No reaction was observed with 10 mol% of Ti(OEt)<sub>4</sub>, Ti(*i*-PrO)<sub>4</sub>, Al(*i*-PrO)<sub>3</sub>, CeCl<sub>3</sub>, FeCl<sub>3</sub>, MgBr<sub>2</sub>, Cu(OAc)<sub>2</sub>, Rh(OAc)<sub>2</sub>, RuCl<sub>3</sub>, or NiCl<sub>2</sub> after a reaction time of 70 h. Traces of the desired rearrangement product 2a together with unreacted imidate 1a, [1,3]-rearrangement product 3a, and trichloroacetamide (4) were obtained in the presence of 10 mol% of  $(CuOTf)_2 \cdot C_6 H_6$ , Cu(OTf)<sub>2</sub>, CuCl, CuCl<sub>2</sub>, and ZnCl<sub>2</sub> within 18–70 hours. The conversion of imidate 1a to amide 2a was slow (ca. 30%, 70 h) with 50 mol% of AgOTf. After attempting such a range of catalysts we were pleased to find that 10 mol% of PtCl<sub>2</sub>, PtCl<sub>4</sub>, AuCl, and AuCl<sub>3</sub> effectively promoted the rearrangement of trichloroacetimidate 1a (Table 1). In the case of PtCl<sub>2</sub>, AuCl, and AuCl<sub>3</sub>, the appropriate solvent was CH<sub>2</sub>Cl<sub>2</sub>, however, PtCl<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub> gave a low yield of product 2a due to competitive formation of the [1,3]-rearrangment product **3a** and elimination of trichloroacetamide (4). The unwanted side reactions in the PtCl<sub>4</sub>-catalyzed rearrangement of imidate 1a were suppressed by changing the solvent to THF and substantially increased the yield of product 2a. The efficiency of the newly found catalysts was explored with additional structurally diverse trichloroacetimidates **1b–e** (Table 1). Imidates 1b and 1c gave the expected Overman rearrangement products 2b and 2c in moderate to good yields. The elimination of trichloroacetamide (4) dominated in the case of imidate 1d, with the trisubstituted double bond and the expected amide 2d formed only in trace amounts.<sup>7</sup> Imidate **1e** derived from (*Z*)-(3-benzyloxy)crotyl alcohol yielded vinyl-oxazolidine 5. Such a product probably forms via a mechanism different to that of the Overman rearrangement, and has been reported also in the PdCl<sub>2</sub>(PhCN)<sub>2</sub>-catalyzed reactions of a similar substrate, bis-trichloroacetimidate, derived from *cis*-butanediol.<sup>8</sup>

Noteworthy, AuCl, AuCl<sub>3</sub>, and  $PtCl_4$  were soluble in solvents selected for the reaction, while  $PtCl_2$  was poorly soluble in both  $CH_2Cl_2$  and THF resulting in hetero-



### Scheme 1

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| Entry | Imidate                        | Product                           | Catalyst <sup>a</sup> | Solvent                         | Yield <sup>b</sup> |
|-------|--------------------------------|-----------------------------------|-----------------------|---------------------------------|--------------------|
| 1     | CCI                            | <u></u>                           | PtCl <sub>2</sub>     | CH <sub>2</sub> Cl <sub>2</sub> | 89%                |
| 2     | l °                            |                                   |                       | THF                             | 83%                |
| 3     | HN                             | HŅ <sup>∽</sup> `CCl <sub>3</sub> | $PtCl_4$              | CH <sub>2</sub> Cl <sub>2</sub> | 30%                |
| 4     | $\sim$                         |                                   |                       | THF                             | 75%                |
| 5     | Me                             | Me                                | AuCl                  | CH <sub>2</sub> Cl <sub>2</sub> | 82%                |
| 6     | 1a                             | 2a                                | AuCl <sub>3</sub>     | $CH_2Cl_2$                      | 80%                |
| 7     | ÇCI <sub>3</sub>               | ö                                 | PtCl <sub>2</sub>     | $CH_2Cl_2$                      | 81%                |
| 8     | , °                            |                                   | PtCl <sub>4</sub>     | THF                             | 56%                |
| 9     | HN <sup>×</sup> <sup>`</sup> Q |                                   | AuCl                  | $CH_2Cl_2$                      | 74%                |
| 19    | Pr                             | Pr                                | AuCl <sub>3</sub>     | $CH_2Cl_2$                      | 71%                |
|       | 1b                             | 2b                                |                       |                                 |                    |
| 11    | CCI                            | 0                                 | PtCl <sub>2</sub>     | CH <sub>2</sub> Cl <sub>2</sub> | 61%                |
| 12    | J - · 3                        |                                   | PtCl                  | THF                             | 28%                |
| 13    | HN                             | HŅ́ ́ ℃CCI₃                       | AuCl                  | CH <sub>2</sub> Cl <sub>2</sub> | 52%                |
| 14    | Ph                             | Ph                                | AuCl <sub>3</sub>     | $CH_2Cl_2$                      | 34%                |
|       | 1c                             | 2c                                |                       |                                 |                    |
| 15    | Ме                             | 0                                 | PtCl <sub>2</sub>     | CH <sub>2</sub> Cl <sub>2</sub> | traces             |
| 16    |                                |                                   | PtCl <sub>4</sub>     | THF                             | traces             |
| 17    | Me                             | HNCCI <sup>3</sup>                | AuCl                  | CH <sub>2</sub> Cl <sub>2</sub> | traces             |
| 18    |                                | Me                                | AuCl <sub>3</sub>     | $CH_2Cl_2$                      | traces             |
|       | 1d                             | 2d                                |                       |                                 |                    |
| 19    | NH                             |                                   | PtCl                  | CH <sub>2</sub> Cl <sub>2</sub> | 83%                |
| 20    |                                | N//                               | AuCl                  | CH <sub>2</sub> Cl <sub>2</sub> | 74%                |
| 21    |                                |                                   | AuCl <sub>3</sub>     | $CH_2Cl_2$<br>$CH_2Cl_2$        | 55%                |
|       |                                | 5                                 |                       |                                 |                    |
|       | 10                             |                                   |                       |                                 |                    |

 Table 1
 PtCl<sub>2</sub>, PtCl<sub>4</sub>, AuCl, and AuCl<sub>3</sub>-Catalyzed Rearrangement of O-Allyltrichloroacetimidates 1a-e

<sup>a</sup> Rearrangement of imidate 1a: 10 mol%; imidates 1b-e: 5 mol%.

<sup>b</sup> Yield of isolated product.

geneous reaction mixtures. The conversion of imidate **1b** was considerably slower using soluble cis-PtCl<sub>2</sub>(PhCN)<sub>2</sub> (Acros) in THF (ca. 30% conversion, 18 h). This was unexpected since PdCl<sub>2</sub>(PhCN)<sub>2</sub> is the most often used form of Pd(II) for Overman and related rearrangements.

A cyclization induced rearrangement (CIR) mechanism has been proposed for the catalytic Overman rearrangement where the metal coordination with the double bond induces a nitrogen addition–deoxymetalation sequence (Scheme 2).<sup>3b</sup> Considering the soft Lewis acid nature of Pt and Au ions,<sup>9</sup> which determines their ability to complex a double bond, it is likely that catalysis by these metal salts also proceeds according to a CIR mechanism. Lowering the oxidation state increases the softness of the metal ion and may account for the higher efficiency of PtCl<sub>2</sub> and AuCl compared to PtCl<sub>4</sub> and AuCl<sub>3</sub> for the rearrangement of imidates **1a–c** and **1e**.



Scheme 2

In summary we have found that  $PtCl_2$ ,  $PtCl_4$ , AuCl, and AuCl\_3 catalyze the rearrangement of *O*-allyl-trichloroacetimidates complementing the known Hg(II) and Pd(II) salts. Further exploration of the utility of these newly found catalysts as well as their incorporation into chiral complexes for the asymmetric Overman rearrangement is currently underway in our group.

### **Typical Procedure**

The reaction vessel was charged with the catalyst (5–10 mol%) under an inert atmosphere and to this a solution of imidate **1a**–e<sup>1b</sup> (1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> or THF (2.2 mL) was added in one portion. The resulting mixture was stirred for 18 h and filtered through a Forisil Plug. The solvent was removed and the product was purified by flash chromatography on silica gel (light petroleum ether–EtOAc). The rearrangement products **2a–c** and **5** are known compounds.<sup>1a,8a</sup>

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