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A Novel Application of $[Cr(en)_2]^{2+}$ in the Synthesis of 1,2-Diols from Aromatic Aldehydes

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A reductive pinacol type arylaldehyde homocoupling process mediated by the $[Cr(en)_2]^{2+}$ complex is described. This procedure affords the *meso*-stereoisomer as the major product, an unexpected result considering that most organometallic methodologies preferentially yield the *dl*-isomer. Additionally, the method represents a novel application of the $[Cr(en)_2]^{2+}$.

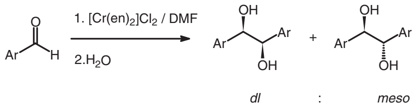
Reductive pinacol type coupling has been an important reaction in organic synthesis since its discovery.[1] Development of new improved reagents for synthetic applications of 1,2-diols constantly appear in the literature, such as a sophisticated vanadium complex for the cross coupling of aromatic aldehydes[2] and an electride which was used in a pinacol coupling reaction in aqueous medium, giving low to moderate yields.[3]

It is worth mentioning that $CrCl_2$ and derived complexes have resulted in useful reagents for many synthetic transformations, mainly C–C coupling reactions and a large amount of information is available.[4] However diol formation is a side process when Cr(II) is used during aldehyde alkylation.[5] Indeed we also observed pinacol coupling during alkylation of aldehydes with $[Cr(en)_2]^{2+}$/DMF.[5c] Strategies aimed to obtain the arylaldehyde dimerization using Cr(II) have involved Zn or Mn powder, chlorosilanes and a catalytic amount of $CrCl_2$ or $CrCl_3$ and chromium complexes such as Cp_2Cr or $(BiPy)_2Cr$. Best yield was given by benzaldehyde (88%), other arylaldehydes dimerized in the range 51–77%.[6] The reductive pinacol type aldehyde homocoupling process is mainly made with other reagents and other transition metals[7] and here the SmI_2 participation is privileged.[8] On the other hand, the $[Cr(en)_2]^{2+}$ complex is an interesting reagent, although it is scarcely used in organic synthesis. This complex was used in the reduction of ω-alkenyl halides to afford cyclic products,[9] it is also a useful reagent for the addition of alkyl halides to electron-deficient alkenes.[10]

Herein, a novel application of the $[Cr(en)_2]^{2+}$ complex in an alternative method for the synthesis of 1,2-diols via arylaldehyde dimerization is described.

Benzaldehyde was reductively dimerized to the corresponding 1,2-diol upon treatment with the $[Cr(en)_2]^{2+}$ complex at room temperature, furnishing the *meso*-isomer as the main product (96%) and only traces of the *dl*-coupling diastereoisomer. An unusual result considering that most of pinacol coupling organometallic mediated processes afford either a 1:1 *meso*–*dl* mixture or the *dl*-isomer as the major product.[6,8,11] Boland obtained 1,2-diphenyl-1,2-ethanediol as 30:70 *dl*:*meso* mixture with Cp_2Cr.[6] Very recently high *meso*-diastereoselectivity in diol formation from aldehydes was attained using aluminum powder/copper sulfate as catalysts.[12]

Table 1. Reductive dimerization of benzaldehyde and substituted aromatic aldehydes



1 2 3

Ar	1,2-diols, **3**[a]	*dl*:*meso* ratio[b]	Total yield[c] /%[d]	Total yield[e] /%[f]
C_6H_5	**3a**	2:98	78[g] (74)	98 (96)
p-CH_3–C_6H_4	**3b**	25:75	57 (42)	98 (73)
p-$(CH_3)_2CH$–C_6H_4	**3c**[h]	2:98	33 (30)	94 (88)
p-CH_3O–C_6H_4	**3d**	2:98	36 (32)	78 (73)
p-Br–C_6H_4	**3e**[i]	25:75	53 (38)	70 (50)
p-CN–C_6H_4	**3f**	25:75	42 (32)	98 (78)
m-CH_3–C_6H_4	**3g**	25:75	65 (45)	96 (73)

[a]The spectroscopic data are in agreement with those reported in the literature.[8a,13,14] [b]Determined by ^1H NMR spectroscopy. [c]Yield *meso*:*dl*. [d](Isolated yield *meso*-isomer), water work up. [e]Yield *meso*:*dl*. [f](Isolated yield *meso*-isomer), aqueous NH_4Cl work up. [g]88% yield determined by ^1H NMR using toluene as internal standard. [h]**3c** is a new compound and it was fully characterized.[15] [i]Reaction was carried out at −10 °C.

$CrCl_2$ and the $[Cr(en)_2]^{2+}$ complex have participated in some processes involving radicals: ω-hexenyl bromide reduction,[9] the trapping of radicals by electron-withdrawing substituted alkenes[10] and the tandem carbon–carbon bond reaction.[16] On these grounds it is possible to assume that radicals are involved in the dimerization reaction at hand. In addition, it is known that sterically crowded radicals predominantly yield *meso*-dimers.[17] Thus, the complex $[Cr(en)_2]^{2+}$ behaves in a similar way as SmI_2, transferring a single electron during the reduction process. Experiments are currently in progress to find out the origin of the *meso*-selectivity.

The dimerization obtained with benzaldehyde prompted the application of the Cr(II) complex on other aromatic aldehydes. Of particular interest were 4-substituted arylaldehydes, since the effect of different electron-donating or electron-attracting contributions to the carbonyl moiety could be evaluated. The result of the reductive process is summarized in Table 1.

It is clear from the table that the $[Cr(en)_2]^{2+}$ complex reductively dimerized aromatic aldehydes to *vic*-diols, with the *meso*-coupling products being preferentially formed. However, electronic contributions from the 4-substituents had no impact on the reaction and consequently no trend was established in the

1,2-diol production. Thus, *p*-tolualdehyde gave a similar yield of the 1,2-diol as *p*-cyanobenzaldehyde, no reduction of the nitrile group by the complex was observed. It is also notable that reductive dimerization was not observed with *p*-nitrobenzaldehyde or *N*,*N*-dimethylaminobenzaldehyde. With the former the corresponding nitrobenzyl alcohol was the sole isolated compound. With the latter, no product was isolated, nor was any starting material recovered. 2-Naphthaldehyde did not react at all and the starting material was fully recovered. 2,4-Dimethylbenzaldehyde and *o*-tolualdehyde did not undergo the reductive dimerization process, instead the corresponding alcohol was isolated, indicating that steric hindrance may be playing an important role during the process, *m*-tolualdehyde did produce the corresponding vicinal diol.

The *meso*-selectivity of 1,2-diphenyl-1,2-ethanediol,[18a] 1,2-bis(*p*-isopropylphenyl)-1,2-ethanediol and 1,2-bis(*p*-methoxyphenyl)-1,2-ethanediol[18b] was further confirmed by X-ray diffraction of the supramolecular structures obtained from each of these diols with imines.

Procedures related to the one herein described include the diastereoselective and enantioselective dimerization of arylaldehydes by $TiCl_2$ in the presence of a variety of enantiopure amines or hydrazine reagents. An example of an *ortho*-aldehyde dimerization has also been reported.[19]

Particularly interesting was a *dl*-diastereoselective pinacol coupling with Ti(III),[17] which showed that aldehydes with electron-withdrawing substituents give better dimerization yields as compared to those substituted with electron donors. The last procedure is in contrast with the results obtained in the present investigation. Thus, it seems that several factors influence the reductive pinacol process,[7,20] including the metal oxidation state, the ligands involved, and the reaction conditions (i.e., temperature).[7,17,21] In our case, experimental procedures are based on the protocol followed in the alkylation of alkenes by Cr(II).[10] The effect of temperature on the process and the use of an accompanying reducing agent to overcome the Cr(II) relative stoichiometric disadvantage of the process will be published in due time. The work up of the reaction at hand was a determining factor in the overall yield. Quenching the reaction with water[10] gave low to moderate yields, while strong acid conditions were avoided, as they would have led to a protonated product more soluble in water. But treatment of the reaction crude with 5% aqueous NH_4Cl solution during 4 h increased the isolation yields (Table 1).

We consider that the method developed in the current study is competitive with those already described in the literature, even with one using aluminum powder/copper sulfate.[12] A methodology for diastereoselective hydrobenzoin synthesis based on the use of the $[Cr(en)_2]^{2+}$ complex was developed. This novel application of the $[Cr(en)_2]^{2+}$ complex predominantly formed *meso*-isomers in yields comparable to those obtained with other organometallic assisted processes. Therefore, this methodology represents an alternative for vicinal diol synthesis, with the advantage that the use of chromium is a simple and inexpensive protocol. Procedures are available in Supporting Information.[15]

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