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Selectivity Control in Nitroaldol (Henry) Reaction by Changing the Basic Anion in a Chiral Copper(II) Complex Based on (*S*)-2-Aminomethylpyrrolidine and 3,5-Di-*tert*-butylsalicylaldehyde

Olga V. Khromova [1], Lidiya V. Yashkina [1], Nadezhda V. Stoletova [1], Victor I. Maleev [1], Yuri N. Belokon [1,*] and Vladimir A. Larionov [1,2,*]

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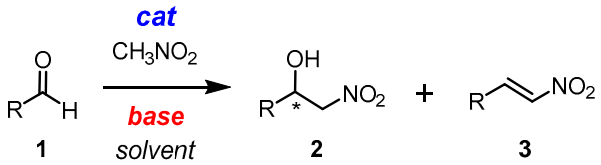
Abstract: This article is a continuation of our previous research on the catalytic capability of chiral copper complex based on commercially available (*S*)-2-aminomethylpyrrolidine and 3,5-di-*tert*-butylsalicylaldehyde with various counter-anions in the asymmetric Henry reaction. Our findings indicate that depending on the type of base used, chiral nitroalcohols with yields up to 97% and *ee* values up to 78%, as well as β-nitrostyrenes with yields up to 82% can be produced. Additionally, it has been found that the outcome of the reaction and the catalytic properties of copper(II) complexes (*S*)-**Cu1** and (*S*)-**Cu2** are influenced by the structure of the aldehyde used.

Keywords: Henry reaction; copper complex; nitroalcohols; nitrostyrenes; enantioselectivity

1. Introduction

The nitroaldol reaction, also known as the Henry reaction [1], is a classical and versatile method for producing chiral β-nitroalcohols **2** (Scheme 1) [2]. These can then be easily converted into a wide variety of valuable products, including α-nitro ketones [3], nitro alkenes [4], β-amino alcohols [5], and alkanes, and even some drugs [6]. Many catalytic systems have been used for this reaction, including the chiral ones [7–11]. In most cases the combination of both Lewis acid and Brønsted base is required for the efficient catalysis of this reaction. Obviously, it is challenging to combine both of these in the same system. Depending on the balance the Brønsted basicity and Lewis acidity of the catalyst, the reaction may also produce dehydration products, such as nitroalkenes **3**, which are also important building blocks in organic synthesis (Scheme 1) [12].



Scheme 1. Henry (nitroaldol) reaction.

Despite the importance of nitroalkenes **3** as diverse building blocks, there have been only a few reports of their formation in the case of using copper complexes as catalysts so far [13]. For example, in 2010, Luo and Yan used a homogenous copper(II) complex based on chiral α-ethylphenyl amines in the asymmetric Henry reaction, and obtained accompanied nitrostyrene products in up to 47% yield under the reaction conditions [13a]. The Jones and Schulz groups showed that immobilizing

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chiral copper(II) complexes on a solid-support also led to the formation of undesired nitroalkenes **3** (up to 35%) [13b,c]. This is likely due to the intrinsic acidity of the silica-based support. However, the systematic and in-depth investigations into the influence of the ligand Brønsted basicity and Lewis acidity of the central metal cations on the selectivity of the aldol condensation have not been explored and assessed.

Here, we set ourselves the task of partially filling this knowledge gap by using chiral copper(II) complexes that we have previously developed [14], derived from the tridentate Schiff bases of (*S*)-2-aminomethylpyrrolidine and 3,5-di-*tert*-butylsalicylaldehyde and different basic anions in the reaction of nitromethane with various aldehydes (Figure 1). We hypothesised that by changing the nature of the basic anions of the complex, we can switch the selectivity of the reaction to obtain either β-nitroalcohol **2** or nitroalkene **3**, both of which are valuable building blocks in synthetic chemistry [2–6].

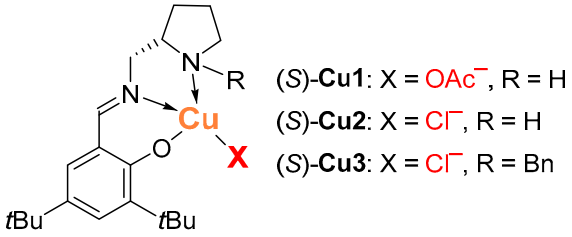


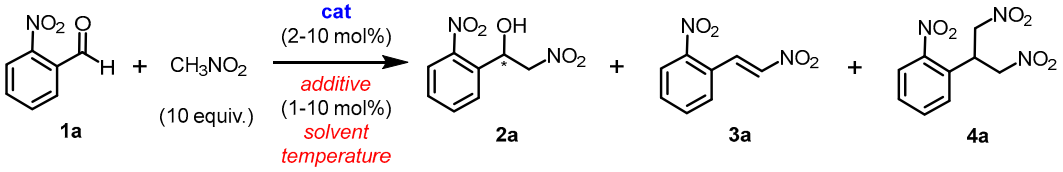
Figure 1. Chiral copper(II) complexes **Cu1-Cu3**.

2. Results and Discussion

2.1. Henry Reaction Conditions Screening

We previously demonstrated that the chiral copper(II) complex (*S*)-**Cu1** catalyzes Henry reaction of *o*-nitrobenzaldehyde **1a** with nitromethane, producing only the nitroalcohol **2a** in 78% yield with 77% *ee* at room temperature (Table 1, entry 1) [14b]. On the other hand, nitrostyrene **3a** was formed in a 55% yield if the temperature was raised to 50 °C in 1,2-dichloroethane (DCE) as a solvent and also the enantiomeric purity of **2a** dropped to 25% (Table 1, entry 2). The yield of product **2a** was significantly increased up to 96% with 73% *ee* using an additional amount of acetate base (Table 1, entry 4).

Table 1. Reaction condition screening for the reaction of *o*-nitrobenzaldehyde **1a** with nitromethane catalyzed by chiral Cu(II) complexes.[a]



entry	catalyst	additive (*x mol%*)	solvent	T, °C	yield (*ee*) of **2a** (%)[b,c]	yield of **3a** (%)[b]	Yield of **4a** (%)[b]
1[ref. 14b]	(*S*)-**Cu1**	–	CD_2Cl_2[d]	RT	78 (77)	–	–
2	(*S*)-**Cu1**	–	DCE	50	43 (25)	55	*traces*
3	(*S*)-**Cu1**	NaOAc (10)	DCE	RT	63 (60)	3	–

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4	(*S*)-**Cu1**	NaOAc (10)	THF/CH_2Cl_2	RT	96 (73)	2	–
5	(*S*)-**Cu2**	-	CH_2Cl_2	RT	NR	–	–
6[f]	(*S*)-**Cu2**	PhONa (10)	CH_2Cl_2	RT	53 (12)	40	3
7	(*S*)-**Cu2**	PhONa (10)	CH_2Cl_2	–17	98 (39)	*traces*	*traces*
8[f]	(*S*)-**Cu2**	Ag_2O (5)	CH_2Cl_2	RT	59 (0)	34	2
9	(*S*)-**Cu2**	Ag_2O (5)	CH_2Cl_2	RT	31 (ND)	54	14
10	(*S*)-**Cu2**	Ag_2O (5)	CH_2Cl_2	–17	89 (56)	4	*traces*
11[f,g]	(*S*)-**Cu2**	Ag_2O (5)	CH_2Cl_2	RT	71 (ND)	24	*traces*
12[g]	(*S*)-**Cu2**	Ag_2O (5)	CH_2Cl_2	RT	50 (ND)	48	2
13	(*S*)-**Cu2**	Ag_2O (5)	DCE	RT	23 (ND)	63	13
14	(*S*)-**Cu2**	Ag_2O (5)	CH_3CN	RT	72 (ND)	16	11
15	(*S*)-**Cu2**	Ag_2O (5)	EtOAc	RT	51 (ND)	30	18
16	(*S*)-**Cu2**	Ag_2O (5)	THF	RT	69 (ND)	15	15
17	(*S*)-**Cu2**	Ag_2O (5)	1,4-dioxane	RT	51 (ND)	32	16
18	(*S*)-**Cu2**	Ag_2O (5)	toluene	RT	28 (ND)	61	10
19	(*S*)-**Cu2**	Ag_2O (5)	MeOH	RT	99 (ND)	–	–
20[h]	(*S*)-**Cu2**	Ag_2O (5)	-	RT	44 (ND)	35	20
21	(*S*)-**Cu2**	Ag_2O (5)	DCE	50	4 (ND)	**81**	14
22	(*S*)-**Cu2**	Ag_2O (5)	DCE	70	<1 (ND)	**81**	18
23	(*S*)-**Cu2** (5)	Ag_2O (2.5)	DCE	70	2 (ND)	**87**	10
24	(*S*)-**Cu2** (2)	Ag_2O (1)	DCE	70	4 (ND)	**87**	8
25[i]	(*S*)-**Cu2** (2)	Ag_2O (1)	DCE	70	3 (ND)	**88**	6

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26[i]	$CuCl_2$*2H_2O + 1,10-phen (2)	Ag_2O (1)	DCE	70	33 (ND)	23	4
27	–	Ag_2O (5)	DCE	50	NR	–	–
28	–	*t*BuOK (5)	DCE	50	85 (0)	–	–
29	(*S*)-**Cu3**	Ag_2O (5)	DCE	50	7 (ND)	78	13
30	(*S*)-**Cu3**	NaOAc (10)	DCE	RT	11 (ND)	72	15

[a]Reaction conditions: *o*-nitrobenzaldehyde **1a** (0.15 mmol), nitromethane (10 eq., 1.5 mmol), catalyst (10 mol%) and an additive (5 or 10 mol%) in 0.5 mL solvent were stirred for 24 h. [b]Yields were determined by ^{1}H NMR analysis of the crude mixture. [c]Enantiomeric excess was determined by chiral HPLC analysis. [d]0.1 equiv. of water was added. [e]1.0 equiv. of water was added. [f]The reaction time was 3 h. [g]CD_3NO_2 was used instead of CH_3NO_2. [h]30.0 equiv. of CH_3NO_2 was used. [i]5.0 equiv. of CH_3NO_2 was used. DCE = 1,2-dichloroethane. NR = no reaction.

Expectedly, the complex (*S*)-**Cu2** with a non-basic chloride anion was catalytically inactive (Table 1, entry 5). Therefore, the next step was to assess the basicity of the anion in the copper(II) complex. In situ exchange of the chloride anion with a strong basic phenolate speeded up the conversion to give 53% of **2a** and 40% of **3a** after 3 h (Table 1, entry 6). A similar outcome was achieved with another strong basic anion O^{2-}, which wasgenerated in situ using Ag_2O (Table 1, entry 8). The increased time of the reaction led to a greater proportion of formed **3a** relative to **2a** (Table 1, entry 9). The reaction performed with deuterated nitromethane gave the product **3a** with lower yield (24%) (Table 1, compare entries 8 and 11). The nature of the solvent played an essential role in the reaction, significantly influencing the outcome (Table 1, entries 13-19). The highest yields of product **3a** were achieved using DCE and toluene with yields of 63% and 61%, respectively (Table 1, entries 13 and 18). The reaction proceeded under solvent-free conditions with 30 equivalents of nitromethane produced nitroalcohol **2a** with 44% yield and nitrostyrene **3a** with 35% yield, along with Michael addition product **4a** in 20% yield (Table 1, entry 20). It is worth noting that reaction in methanol using the catalytic system (*S*)-**Cu2**/Ag_2O gave only nitroalcohol **2a** in a quantitative yield (99%) (Table 1, entry 19).

Next, the impact of temperature on the reaction outcome was studied (Table 1, entries 7, 10, 21, 22). Lowering the temperature to –17 °C increased the yield of product **2a** (98% for PhONa and 89% for NaOAc) with a trace amount of **3a** formed; however, the enantioselectivity of the reaction was reduced (Table 1, entries 7 and 10). On the other hand, when the reaction was carried out at 50 °C, the yield of product **3a** increased to 81% (Table 1, entry 21). The further increase in temperature to 70 °C yielded the desired β-nitrostyrene **3a** with 81% yield, although the yield of the *bis*-coupling product **4a** increased to 18% yield (Table 1, entry 22). Then, the decrease in catalyst and $MeNO_2$ loadings was investigated (Table 1, entries 22-25). The maximum yield of nitrostyrene **3a** (88%) was obtained with 2 mol% of the complex (*S*)-**Cu2** and 1 mol% of Ag_2O and 5 equivalents of $MeNO_2$ used (Table 1, entry 25).

For comparison purposes, the reaction using a catalytic system $CuCl_2$/1,10-phenanthroline/Ag_2O was studied under the optimized conditions, and the yield of **3a** was only 23% as compared to 88% in case of (*S*)-**Cu2** (Table 1, entry 26). This demonstrates the superiority of our new system. It should be noted that pure silver oxide does not catalyze the reaction itself (Table 1, entry 27). In contrast, the reaction catalyzed by *t*BuOK resulted in the formation of only nitroalcohol **2a** in 85% conversion (Table 1, entry 28). *N*-benzylated complex (*S*)-**Cu3** influenced the outcome of the reaction (Table 1,

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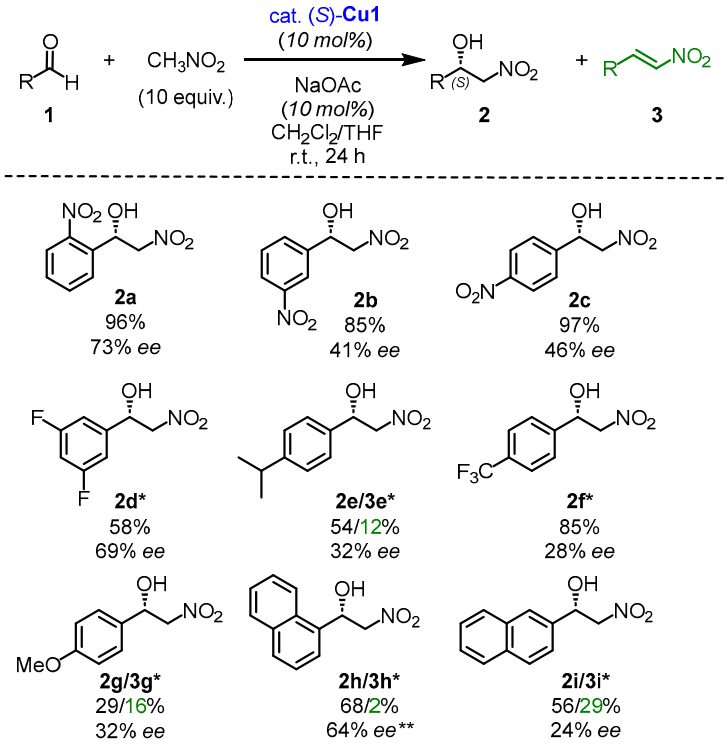
entries 29 and 30). Whereas the yield of nitroalcohol **2a** was low (7% and 11%) and nitrostyrene **3a** became the main product (72% and 78%) (Table 1, entries 29 and 30).

This demonstrates the superiority of our new catalytic system, the selectivity of which is easily modified by simple modification of the tridentate ligand and the nature of the mono-anion.

*2.2. The Scope of Aldehydes in the Enantioselective Henry Reaction with the Complex (S)-**Cu1***

The next step was to examine the reactivity of various aldehydes in the enantioselective Henry reaction promoted by (*S*)-**Cu1** (Scheme 2). The experiments conducted demonstrated that the substituents in the aromatic rings of the aldehydes significantly impacted the yields of the product **2** and **3**. The catalyst (*S*)-**Cu1** demonstrated good activity with benzaldehyde containing electron-withdrawing group (EWG). The *ortho*-, *meta*- and *para*-NO_2-substituted nitroalcohols **2a**-**2c** were produced in high yields (85–97%) with no traces of nitrostyrene observed. A similar pattern was observed for fluorine substituted benzaldehydes, resulting in **2d** with 58% yield and **2f** with 85% yield, respectively. On the other hand, for aldehydes with electron-donating groups (EDG), the targeted Henry reaction was accompanied with the dehydration process. The resulting products **2e**, **2g**-**2i** were isolated in moderate yields (54%, 29%, 68% and 56%, respectively), accompanied by the formation of nitrostyrenes **3e**, **3g**-**3i** (12%, 16%, 2% and 29% yields, respectively). The level of enantioselectivity for the nitroalcohols **2a**-**2i** was moderate (24–73% *ee*).



Scheme 2. Henry reaction catalyzed by the complex (*S*)-**Cu1**. Reaction conditions: aldehyde **1** (0.3 mmol), nitromethane (10 equiv., 3 mmol), complex (*S*)-**Cu1** (10 mol%) and NaOAc (10 mol%) in 0.5 mL of solvent mixture (CH_2Cl_2/THF) were stirred for 24 h. The yields were determined by ^{1}H NMR analysis of the crude mixture using HMDSO as a standard. *The reaction time was 36 h. **No base was used.

2.3. The Scope of Aldehydes in the Synthesis of β-Nitrostyrenes **3**

Next, the Henry reaction protocol was extended using different aldehydes under the conditions with a catalytic system (*S*)-**Cu2**/Ag_2O that favored the formation of nitrostyrene **3** (Scheme 3). The selectivity and efficiency of the catalytic system were also found to be highly sensitive to the structure of **1**. The reaction exhibited a high conversion for aldehydes **1a**-**1e** with nitrostyrene **3** as the

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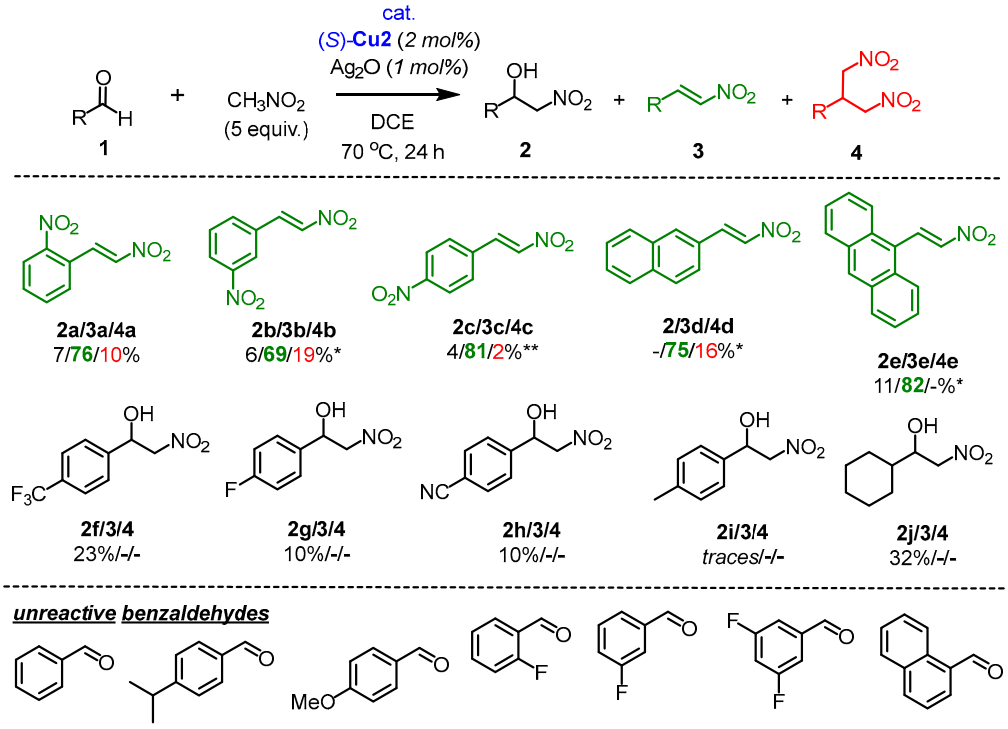
predominant product (*o*-NO_2 **3a**: 76%, *m*-NO_2 **3b**: 69%, *p*-NO_2 **3c**: 81%, 2-naphthyl **3d**: 75% and 9-anthracenyl **3e**: 82%, respectively) (Scheme 3). Importantly, the corresponding *trans*-β-nitrostyrenes **3a**-**3e** were isolated in pure form by crystallization in yields of 74%, 58%, 62%, 58% and 74% respectively. A low conversion and the formation of nitroalcohols with yields up to 32% were observed for aldehydes **1f**-**1j** (Scheme 3). On the other hand, for certain reasons some aldehydes (depicted in Scheme 3) were inactive under the conditions. Most likely, the rate of the retro-nitroaldol reaction was faster as compared to the irreversible dehydration step (*vide infra*). Thus, it seems reasonable to suggest that the (*S*)-**Cu2** complex requires particularly strong EWG groups in the benzaldehyde structure (such as NO_2) in order to achieve efficient catalysis. Even with CF_3 and CN groups, the catalytic activity of (*S*)-**Cu2** was already limited.



Scheme 3. Henry reaction catalyzed by a catalytic system (*S*)-**Cu2**/Ag_2O. Reaction conditions: aldehyde **1** (0.3 mmol), nitromethane (5 equiv., 1.5 mmol), complex (*S*)-**Cu2** (2 mol%) and Ag_2O (1 mol%) in 1 mL of DCE were stirred for 24 h at 70 °C. *(*S*)-**Cu2** (5 mol%), Ag_2O (2.5 mol%), CH_3NO_2 10 equiv. **The reaction time is 48h.

2.4. Mechanism Related Experiments

In order to understand the mechanism of the addition of nitromethane to benzaldehydes and the subsequent dehydration process, a series of retro-nitroaldol experiments were conducted under standard condensation conditions (Scheme 4). The racemic nitroalcohol **2a** was kept in a solution of DCE with a strong base *t*BuOK for 24 h at 50 °C. This caused the complete decomposition of the nitroalcohol into the initial aldehyde **1a** (97% conversion). A similar pattern is evident when DBU is used as the organic base. However, in this case, the conversion remained incomplete (68%). Silver oxide was not effective in the decomposition of nitroalcohol or its dehydration process. As expected, only the combined system (*S*)-**Cu2**/Ag_2O was able to produce a high yield of nitrostyrene **3a** (76%), along with the reverse reaction product – aldehyde **1a** – in 21% (Scheme 4).

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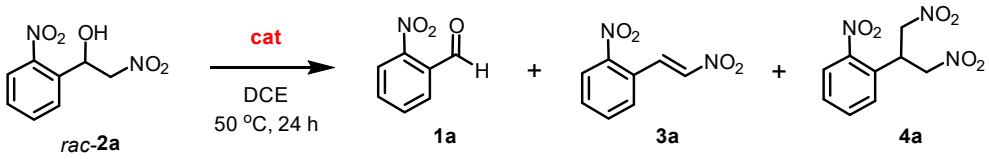

cat.	conv. (%)	**1a** (%)	**3a** (%)	**4a** (%)
(*S*)-**Cu2** (*10 mol%*) + Ag_2O (*5 mol%*)	98	21	76	<1
Ag_2O (*5 mol%*)	4	4	traces	-
DBU (*10 mol%*)	68	64	2	<1
*t*BuOK (*10 mol%*)	97	93	2	2

Scheme 4. Control experiments.

^{1}H NMR kinetic studies of the condensation reaction between benzaldehyde **1a** and CH_3NO_2 and deuterated CD_3NO_2 in CD_2Cl_2 were also conducted (Figure 2). According to the data, the aldol condensation step of the reaction showed a kinetic isotope effect (k_D/k_H) of approximately 10 and 3 for the dehydration process. The result corroborated the involvement of the C-D bond cleavage in the rate limiting stages of both reactions.

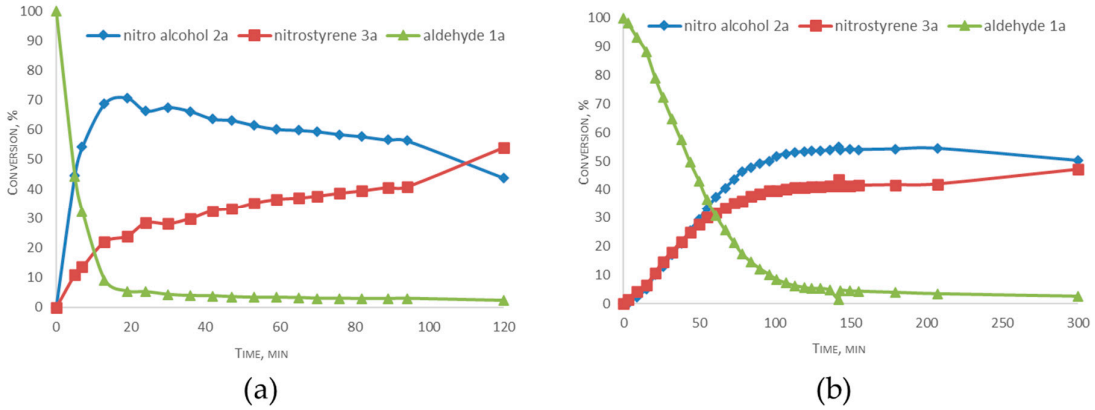

Figure 2. Kinetic profiles of the reaction with nitromethane (*a*) and deuterated nitromethane (*b*) in CD_2Cl_2.

Finally, based on the experimental results and findings, we have proposed a mechanism of the catalysis (Scheme 5). The first step is the formation of a catalytically active dimeric complex from (*S*)-**Cu2** and Ag_2O, where two units of copper complex are linked by a μ^2-oxygen bridge ([L-Cu]-O-[L-Cu]). This catalytic particle with a higher basicity of the oxygen bridge, promotes the reversible nitroaldol reaction, leading to the formation of nitroalcohol **2**. Subsequently, the dehydration process was accelerated as the complex [L-Cu]-O-[L-Cu] appeared to coordinate with product **2**, increasing the acidity of its β-protons and activating the leaving hydroxyl groups of nitroalcohols by coordinating to Cu ion and thus facilitating the E1cB elimination step for the production of β-nitrostyrene **3** (Scheme 5). This concept rationalized why strongly basic ^{t}BuONa promoted only the retro-aldol decomposition of nitroalcohols and not their dehydration. It should also be noted that the Michael addition of the second nitromethane molecule results in the formation of a minor *bis*-coupling product **4** [15].

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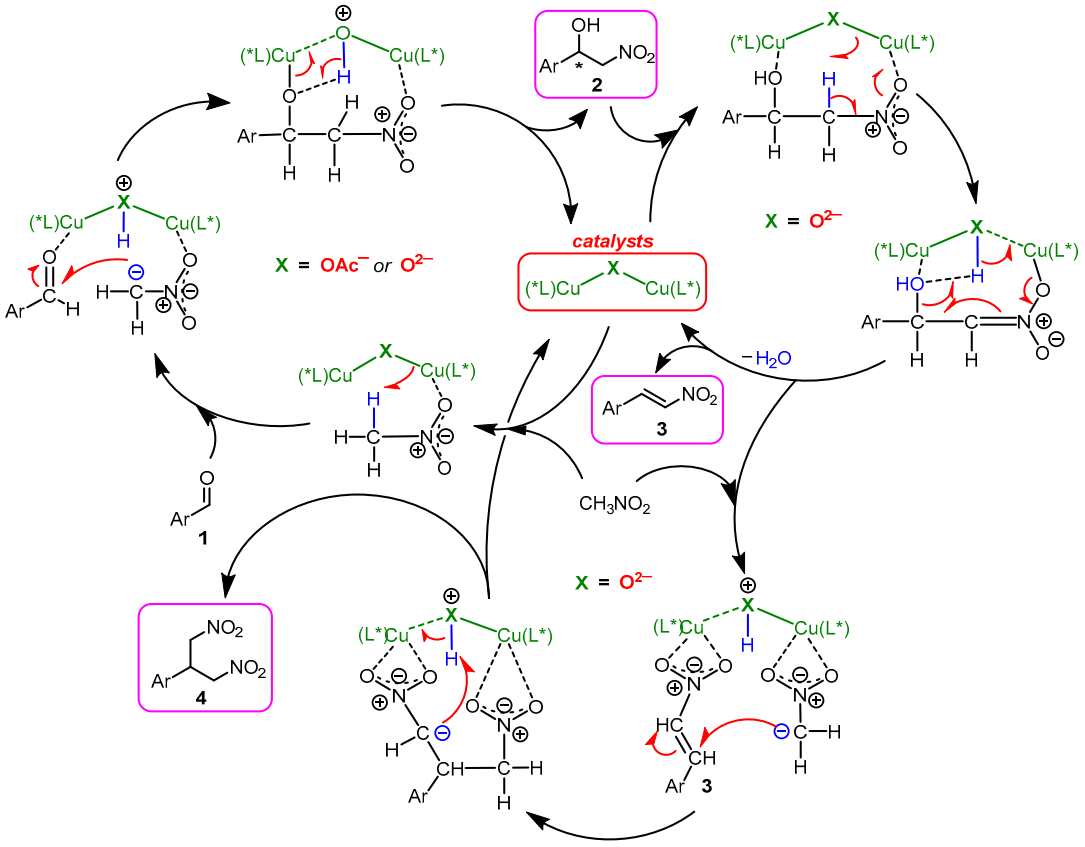

Scheme 5. Proposed mechanism for Henry and subsequent reactions catalyzed by the system (*S*)-**Cu2** and Ag_2O.

3. Materials and Methods

3.1. General Information

All solvents purchased from commercial suppliers were used without further purification (CH_2Cl_2, DCE, MeOH, 1,4-dioxane, $CDCl_3$, CD_2Cl_2, acetone-d_6). THF and toluene were distilled over sodium under an atmosphere of argon. Purchased (*S*)-(2-aminomethyl)pyrrolidine, 3,5-di-*tret*-butylsalicylaldehyde, nitromethane, DBU, CD_3NO_2, *t*BuOK, NaOAc, Ag_2O, $Cu(OAc)_2$ from commercial suppliers were used without further purification. Commercially available benzaldehydes were purified by distillation under reduced pressure or through SiO_2 short column. (*S*)-2-aminomethyl-1-benzylpyrrolidine were synthesised according to a literature procedure starting from 1-benzyl-(*S*)-proline [16]. The (*S*)-**Cu1**, (*S*)-**Cu2** and (*S*)-**Cu3** complexes were synthesized according to our previously published procedure [14]. The reported catalytic reactions were performed under an atmosphere of argon using Schlenk-line techniques in flame-dried glassware. If not stated otherwise, flash column chromatography was performed with silica gel 60 M from Macherey-Nagel.

3.2. Instrumentation

Proton nuclear magnetic resonance (^{1}H NMR) spectra was recorded on a Bruker Avance 300 NMR spectrometer (operating at 300 MHz respectively referring to ^{1}H nucleus). Chemical shifts are reported in ppm relative to the residual solvent peak ($CDCl_3$: δ = 7.26 ppm for ^{1}H NMR). NMR data are reported as follows: chemical shift, multiplicity (br. s = broad singlet, s = singlet, d = doublet, dd = doublet of doublets, m = multiplet), coupling constant, integration, and nucleus. Chiral HPLC chromatography was performed with a Shimadzu LC-10ADVP instrument equipped with a

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Shimadzu SPDM10AVP diode array detector using a Chiralcel OD-H or Astec Cellulose DMP column (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C).

3.3. Synthesis

3.3.1. General Procedure for the Enantioselective Henry Reaction

A flask (10 mL) was charged with aldehyde **1** (0.3 mmol, 1 equiv.), (*S*)-**Cu1** catalyst (13.2 mg, 10 mol %) and NaOAc (2.4 mg, 10 mol %.) under Ar atmosphere. Then, solvent mixture (THF (0.25 mL)/DCM (0.25 mL)) and nitromethane (0.160 mL, 3 mmol, 10 equiv.) were added and the reaction mixture was stirred for 24 h at RT. After completing of the reaction, the reaction mixture was purified by flash SiO_2 chromatography (eluent: CH_2Cl_2). The solvent was evaporated on a rotary evaporator, and the residue was purified by column SiO_2 chromatography (eluent: hexane/acetone (5:1)) to afford the desired product **2**.

1-(2-nitrophenyl)-2-nitroethan-1-ol (**2a**)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 1H, ArH), 7.98–7.96 (m, 1H, ArH), 7.78–7.74 (m, 1H, ArH), 7.59–7.55 (m, 1H, ArH), 6.07 (ddd, *J* = 8.8, 4.2, 2.2 Hz, 1H), 4.89 (dd, *J* = 13.9, 2.2 Hz, 1H), 4.57 (dd, *J* = 13.9, 8.8 Hz, 1H), 3.15 (d, *J* = 4.2 Hz, 1H) ppm.
All spectroscopic data were in agreement with the literature [14b].
The enantiomeric excess was established by HPLC analysis using a Kromasil 3-AmyCoat column, *ee* = 73% (conditions: heptane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 12.7 min, t_R(minor) = 11.0 min).
All spectroscopic data were in agreement with the literature [14a].

1-(3-nitrophenyl)-2-nitroethan-1-ol (**2b**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.33–8.28 (m, 1H), 8.24–8.15 (m, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.64–7.56 (m, 1H), 5.66–5.55 (m, 1H), 4.68–4.54 (m, 2H), 3.46–3.40 (m, 1H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 41% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 28.4 min, t_R(minor) = 25.0 min).
All spectroscopic data were in agreement with the literature [17a].

1-(4-nitrophenyl)-2-nitroethan-1-ol (**2c**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.26 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 5.65–5.56 (m, 1H), 4.67–4.51 (m, 2H), 3.33–3.26 (m, 1H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 46% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 31.4 min, t_R(minor) = 25.3 min).
All spectroscopic data were in agreement with the literature [17a].

1-(3,5-difluorophenyl)-2-nitroethan-1-ol (**2d**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.02–6.91 (m, 2H), 6.85–6.74 (m, 1H), 5.51–5.41 (m, 1H), 4.62–4.46 (m, 2H), 3.14–3.07 (m, 1H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –107.7 (s, 2F) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 69% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 12.5 min, t_R(minor) = 10.7 min).
All spectroscopic data were in agreement with the literature [17b].

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1-(4-isopropylphenyl)-2-nitroethan-1-ol (**2e**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.30 (m, 2H), 7.29–7.23 (m, 2H), 5.48–5.39 (m, 1H), 4.61 (dd, *J* = 13.3, 9.6 Hz, 1H), 4.50 (dd, *J* = 13.2, 3.1 Hz, 1H), 3.00–2.86 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 6H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 32% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 18.2 min, t_R(minor) = 12.2 min).
All spectroscopic data were in agreement with the literature [17c].

1-(4-(trifluoromethyl)phenyl)-2-nitroethan-1-ol (**2f**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.67 (d, *J*=8.1 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 5.60–5.48 (m, 1H), 4.65–4.48 (m, 2H), 3.21–3.09 (m, 1H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.7 (s, 3F) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 28% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 14.6 min, t_R(minor) = 11.5 min).
All spectroscopic data were in agreement with the literature [17a].

1-(4-methoxyphenyl)-2-nitroethan-1-ol (**2g**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.35–7.28 (m, 2H), 6.95–6.89 (m, 2H), 5.45–5.37 (m, 1H), 4.60 (dd, *J* = 13.2, 9.6 Hz, 1H), 4.47 (dd, *J* = 13.2, 3.1 Hz, 1H), 3.81 (s, 3H), 2.84–2.80 (m, 1H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 32% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 26.0 min, t_R(minor) = 20.3 min).
All spectroscopic data were in agreement with the literature [17a].

1-(naphthalen-1-yl)-2-nitroethan-1-ol (**2h**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.04 (d, *J* = 8.3 Hz, 1H), 7.94–7.89 (m, 1H), 7.89–7.83 (m, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.64–7.49 (m, 3H), 6.30–6.23 (m, 1H), 4.74–4.59 (m, 2H), 2.92 (d, *J*=3.6 Hz, 1H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 64% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 24.8 min, t_R(minor) = 18.0 min).
All spectroscopic data were in agreement with the literature. [17c]

1-(naphthalen-2-yl)-2-nitroethan-1-ol (**2i**)
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.90–7.81 (m, 4H), 7.57–7.49 (m, 2H), 7.49–7.41 (m, 1H), 5.65–5.56 (m, 1H), 4.68 (dd, *J* = 13.3, 9.4 Hz, 1H), 4.57 (dd, *J* = 13.3, 3.2 Hz, 1H), 3.16–3.10 (br. s, 1H) ppm.
The enantiomeric excess was established by HPLC analysis using a Chiralcel OD-H column, *ee* = 24% (conditions: hexane/isopropanol = 90:10, flow rate: 1 mL/min, 254 nm, 25 °C, t_R(major) = 52.5 min, t_R(minor) = 37.1 min).
All spectroscopic data were in agreement with the literature. [17b]

3.3.2. General Procedure for the Synthesis of β-Nitrostyrenes **3**

A flask (10 mL) was charged with aldehyde **1** (0.3 mmol, 1 equiv.), complex (*S*)-**Cu2** (2.4 mg, 2 mol% or 6.2 mg, 5 mol%) and Ag_2O (0.7 mg, 1 mol% or 1.8 mg, 2.5 mol%). Then, 1,2-dichloroethane (1 mL), nitromethane (0.08 mL, 1.5 mmol, 5 equiv. or 0.16 mL, 3.0 mmol, 10 equiv.) were added and the reaction mixture was stirred for 24 h at 70 °C. After completing of the reaction, the reaction mixture was filtrated through the SiO_2 layer using CH_2Cl_2 as an eluent. The solvent was evaporated on a rotary evaporator, and the residue was purified by column SiO_2 chromatography or by crystallization in ethanol to afford the desired product **3**.

2-nitro-β-nitrostyrene (**3a**)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 13.4 Hz, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 7.81–7.65 (m, 2H), 7.61 (d, *J* = 7.3 Hz, 1H), 7.43 (d, *J* = 13.5 Hz, 1H) ppm.
All spectroscopic data were in agreement with the literature [18].

3-nitro-β-nitrostyrene (**3b**)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.42 (t, *J* = 2.0 Hz, 1H), 8.35 (dd, *J* = 8.4, 2.2 Hz, 1H), 8.06 (d, *J* = 13.7 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.74–7.63 (m, 2H) ppm.
All spectroscopic data were in agreement with the literature [19].

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4-nitro-β-nitrostyrene (**3c**)
^{1}H NMR (300 MHz, acetone-d_6): δ = 8.33 (d, J = 8.8 Hz, 2H), 8.25–8.07 (m, 4H) ppm.
All spectroscopic data were in agreement with the literature [18].

(E)-2-(2-nitrovinyl)naphthalene (**3d**)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (d, J = 13.6 Hz, 1H), 8.00 (s, 1H), 7.88 (dt, J = 9.4, 3.6 Hz, 3H), 7.69 (d, J = 13.6 Hz, 1H), 7.65–7.51 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.4, 137.3, 135.0, 133.3, 132.4, 129.5, 129.0, 128.5, 128.1, 127.7, 127.4, 123.4 ppm.

(E)-9-(2-nitrovinyl)anthracene (**3e**)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.98 (d, J = 13.7 Hz, 1H), 8.53 (s, 1H), 8.11 (dd, J = 39.5, 8.4 Hz, 4H), 7.76–7.39 (m, 5H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.8, 135.8, 131.2, 130.6, 130.0, 129.3, 127.6, 125.8, 124.4, 123.3 ppm.

5. Conclusions

In conclusion, we have shown that a chiral copper(II) complex prepared from a Schiff base ligand based on commercially available (*S*)-2-aminomethylpyrrolidine and 3,5-di-*tert*-butylsalicylaldehyde can selectively catalyze the Henry reaction, depending on the type of the anion, producing either nitroalcohols or nitrostyrenes. In particularly, the chiral complex containing the acetate anion allows the formation of nitroalcohols with up to 97% yield and *ee* value of up to 78%. On the other hand, the in situ formed catalytic system [L-Cu]-O-[L-Cu] gives predominantly access to β-nitrostyrenes with up to 88% yield. Additionally, it was found that the substituents in the aromatic rings of the aldehydes have a significant impact on the reaction outcome and the formation of nitroolefins. Our results clearly demonstrate that the selectivity of a copper(II) complex can be easily altered by simply modifying the tridentate ligand and the nature of the basic anion.

Supplementary Materials: ^{1}H, ^{13}C and ^{19}F NMR spectra for all compounds, and HPLC traces of the products can be downloaded at website of this paper posted on Preprints.org.

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