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Synthesis of (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol from its Schiff Base by Catalytic Hydrogenation over Palladium

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Abstract: A chiral 1,2-amino alcohol derivative, (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (**BAB**), was synthesized from its Schiff base by catalytic hydrogenation over palladium on carbon, in various solvents (toluene, methanol, hexane, dichloromethane, tetrahydrofuran, ethyl acetate), under mild conditions (room temperature, atmospheric pressure). Preparation of the Schiff base was also optimized. This compound is a resolving agent for preparing optically active, practically important cyclopropanecarboxylic acids.

Keywords: Heterogeneous catalysis, hydrogenation, palladium, supported metal catalyst.

1. INTRODUCTION

Chiral 1,2-amino alcohols are common structural patterns found in a wide range of natural and biologically active molecules [1]. These compounds are useful precursors of various chiral oxazolidinones [2], oxazolines [3] or phosphonamides [4], and they are applied as catalyst ligands or chiral auxiliaries in relevant stereoselective reactions, such as hydrogenation of carbonyl compounds [5, 6] or alkylation of enolates [7, 8], respectively. Furthermore, they can also be used as resolving agents [9].

In this work the liquid-phase heterogeneous catalytic hydrogenation of a Schiff base, (*S*)-(+)-2-(*N*-benzylidineamino)butan-1-ol (**BDAB**), to (*S*)-(+)-2-(*N*-benzylamino)-butan-1-ol (**BAB**) over palladium was investigated in detail. **BAB** proved to be an efficient resolving agent in the optical resolution of practically important cyclopropanecarboxylic acids, such as *cis*- and *trans*-permethric acid (*cis*- and *trans*-3-(2',2'-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid), based on diastereomeric salt formation using traditional methods [10-12] or new ones in supercritical carbon dioxide [13, 14].

Few examples have been reported on the heterogeneous catalytic hydrogenation of **BDAB** and its antipode [15-18], or other optically active Schiff bases prepared from (*R*)-(–)-2-aminobutan-1-ol [19]. Thus, 2-(*N*-benzylidineamino)butan-1-ol was converted to 2-(*N*-benzylamino)butan-1-ol with 68% yield, over 5% Pd/C (catalyst/substrate ratio=0.1), in ethanol, under 3.5 bar hydrogen pressure and at room temperature [15]. Similarly, (*R*)-(–)-2-(*N*-benzylidineamino)-butan-1-ol was hydrogenated to (*R*)-(–)-2-(*N*-benzylamino)-butan-1-ol with 77% yield, over 5% palladium on carbon (3% by weight of substrate), in ethyl acetate, under 1 bar hydrogen pressure, at room temperature [16], while in isopropyl alcohol, applying 0.02 catalyst/substrate ratio, 89% yield was obtained at 70 °C for 24 hrs [17]. Using a direct-reductive-amination (DRA) method [18], the hydrogenation of 2-(*N*-benzylidineamino)butan-1-ol with 10% Pd/C, in methanol, in the presence of $CHCl_3$ (6 v/v%), at room temperature and atmospheric pressure resulted in 97% yield of 2-(*N*-benzylamino)butan-1-ol hydrochloride, namely hydrogen chloride was formed from chloroform due to the hydrodehalogenating ability of palladium. This process, however, has a disadvantage: it uses a non-environmentally benign, chlorinated additive ($CHCl_3$).

Further reduction methods were also applied for the saturation of C=N bond of the Schiff base using sodium borohydride [20-24] or sodium cyanoborohydride [25] as reducing agents. For example, **BDAB** was reduced to **BAB** with $NaBH_4$, in methanol, at 0 °C with 92% yield [21], while in ethanol 88% yield was obtained [22]. Whereas, it is inexpedient to apply sodium borohydride or cyanoborohydride, because they are harmful and expensive reagents, moreover the atom efficiency of this process (72%) is worse than that of the catalytic hydrogenation (100%). In addition, a large amount of hazardous waste is formed during the working-up procedure of the reaction mixture, which requires further destroying treatments.

Direct benzylation of (*S*)-(+) or (*R*)-(–)-2-aminobutan-1-ol with benzyl bromide [26-29] or benzyl chloride [30] could be an alternative route for preparing the target compound. Thus, (*R*)-(–)-2-(*N*-benzylamino)butan-1-ol was prepared from (*R*)-(–)-2-aminobutan-1-ol using benzyl bromide, in boiling toluene, in the presence of Na_2CO_3 with 87% yield

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[26], while that of benzyl chloride the product was isolated with 94% yield [30]. However, due to the formation of HBr or HCl which have to be neutralized by sodium carbonate, a large amount of by-products can be formed increasing the environmental load.

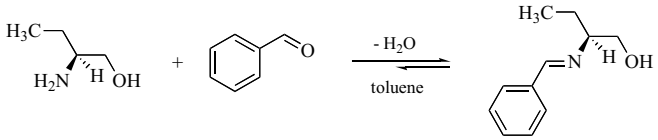
An interesting electrocatalytic method was also used for the synthesis of (*R*)-(–)-2-(*N*-benzylamino)butan-1-ol [31]. Benzylamine was reacted with (*R*)-(–)-2-aminobutan-1-ol in methanol, in the presence of electrogenerated *o*-iminoquinone amine oxidase, at a Pt anode/Hg cathode couple to give the product with 70% yield. Obviously, the use of mercury is the main disadvantage of this process from both practical and environmental points of view.

In this paper the preparation of the Schiff base, the effects of its purity, catalyst/substrate ratio, solvents on the selectivity to **BAB**, as well as on the conversion and the rate of the hydrogenation of **BDAB** are discussed.

2. RESULTS AND DISCUSSION

2.1. Preparation of the Schiff Base

As well known [32, 33], the formation of a Schiff base is a reversible reaction, but the equilibrium can be shifted toward the product by removing water from the reaction mixture. In our case, the Schiff base [(*S*)-(+)-2-(*N*-benzylideneamino)butan-1-ol (**BDAB**)] was synthesized from (*S*)-(+)-2-aminobutan-1-ol (**AB**), an important intermediate of the antimycobacterial Ethambutol [34], and benzaldehyde (**BA**) (Scheme **1**).



AB **BA** **BDAB**

(Scheme **1**). Formation of the Schiff base (**BDAB**) from (*S*)-(+)-2-aminobutan-1-ol (**AB**) and benzaldehyde (**BA**).

The effect of reaction conditions used in the preparation of **BDAB** on the isolated yield and purity of the product is summarized in (Table **1**).

Table 1. Preparation of the Schiff base (BDAB) under different conditions.

Entry	Solvent	Temperature (°C)	Isolated Yield (%)	BDAB Content (%)
1	methanol	25	94	96.1
2	toluene	25	86	94.4
3	toluene	50	96	98.2

Conditions: 0.89 g (10 mmol) (*S*)-(+)-2-aminobutan-1-ol, 1.06 g (10 mmol) benzaldehyde, 35 cm^3 solvent, reaction time: 10 min.

As seen, the highest isolated yield (96%) and purity (98.2%) of **BDAB** were obtained in toluene and at 50 °C, after 10 min reaction time (Table **1**/Entry 3). Without heating, at 25 °C, the starting materials were not able to dissolve completely into toluene, therefore the isolated yield decreased significantly (96 → 86%) and the **BDAB** content became lower (98.2 → 94.4%) (Table **1**/Entry 2). In methanol and at room temperature, both the isolated yield (94%) and the purity (96.1%) values were slightly worse than in toluene (Table **1**/Entry 1), despite the good solubility of the reactants. It is noteworthy, that evaporation of the organic solvents used, under vacuum, was carried out at 50 °C and for 30 min to remove the traces of water, as well.

According to our results, it is expedient to carry out this reaction in toluene and at 50 °C to achieve the highest isolated yield and purity of (*S*)-(+)-2-(*N*-benzylideneamino)butan-1-ol. Furthermore, it is favourable to apply a slight excess of benzaldehyde (~1%) during the preparation of this Schiff base, because the optically active (*S*)-(+)-2-aminobutan-1-ol itself could also act as a resolving agent and it could modify the efficiency of the final product in a resolving process.

2.2. Hydrogenation of the Schiff Base

2.2.1. Reaction Pathway

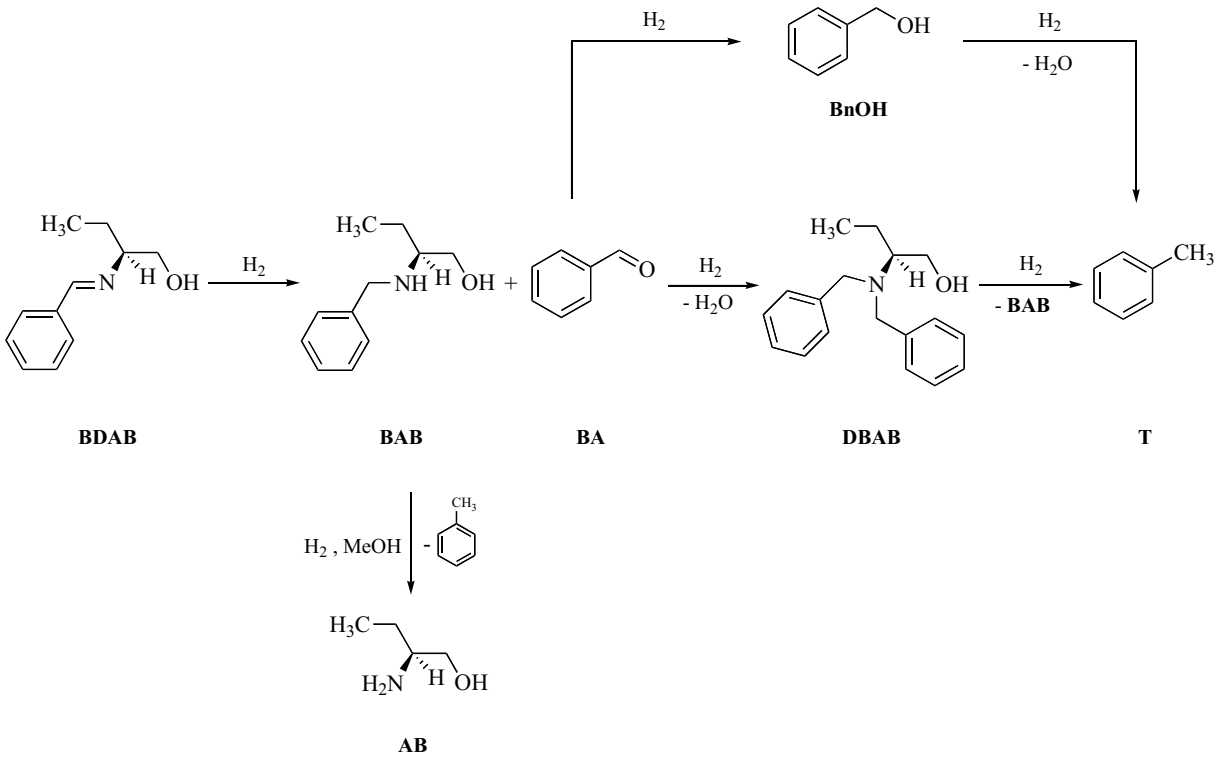
The possible reaction pathways, intermediates and products in the hydrogenation of the Schiff base (**BDAB**) are shown in (Scheme **2**). Formation of (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (**BAB**) takes place by hydrogenation of **BDAB**, but a tertiary amine derivative, (*S*)-(+)-2-(*N,N*-dibenzylamino)butan-1-ol (**DBAB**), can be formed in a coupling reaction of **BAB** and the excess of benzaldehyde (**BA**) accompanied by elimination of water and followed by hydrogenation. Toluene (**T**) and **BAB** can also be formed in a hydrogenolytic step from **DBAB**. Furthermore, **BA** can be hydrogenated to benzyl alcohol (**BnOH**) which also undergoes hydrogenolysis to give toluene.

In methanol, however, a further side-reaction can take place, because the debenzylation of **BAB** can result in (*S*)-(+)-2-aminobutan-1-ol (**AB**) and toluene, but this hydrogenolysis usually takes place under pressure.

2.2.2. Effect of Purity of the Schiff Base

The results of the hydrogenation of **BDAB** prepared in different ways, over 10% Pd/C catalyst (Selcat Q) are given in (Table **2**).

Although in methanol, without preparing the Schiff base, the complete reduction of **BDAB** took place fast, both the purity of product (92.0% **BAB** content) and the selectivity to **BAB** (82%) became significantly lower than in toluene (98.9 and 84%, respectively), while similar isolated yields were obtained (85–89%) (Table **2**/Entries 1 and 4). In case of prepared Schiff base, in methanol again, the reaction also started very fast, as seen in (Fig. **1**), whereas the rate of the hydrogen uptake decreased after 10 min. Moreover, the purity of product, the isolated yield and the selectivity values further diminished (92.0 → 88.3%, 89 → 85%, as well as 82 → 75%) (Table **2**/Entry 2). According to the GC–MS measurements, this was due to (*S*)-(+)-2-aminobutan-1-ol formed in a higher amount (6–8%), namely the *N*-debenzylation of **BAB** took place partly in methanol, even at atmospheric pressure and room temperature, but that of secondary amines, in general, requires higher pressure (>4 bar) and temperature (>40 °C) [35]. Applying toluene the purity of product, irrespectively of the preparation method of the



(Scheme **2**). Reaction pathways in the hydrogenation of (*S*)-(+)-2-(*N*-benzylideneamino)butan-1-ol (**BDAB**).

Table 2. Hydrogenation of the Schiff base (BDAB) prepared in different ways.

Entry	Solvent	Reaction Time for Complete Conversion (min)	Isolated Yield (%)	BAB Content (%)	Selectivity (%)	v_0 (mmol H_2 $mmol_{Pd}^{-1}$ min^{-1})
1[a]	methanol	17	89	92.0	82	2.35
2[b]	methanol	30	85	88.3	75	3.17
3[c]	toluene	25	84	97.8	82	1.66
4[d]	toluene	30	85	98.9	84	1.91

Conditions: 1.70 g Schiff base, 0.34 g 10% Pd/C catalyst (Selcat Q), 30 cm^3 solvent, atmospheric pressure, 25 °C.

[a] Schiff base was not prepared.

[b] Schiff base was prepared.

[c] Schiff base was prepared at 25 °C.

[d] Schiff base was prepared at 50 °C.

Schiff base, was very high (97.8 and 98.9% **BAB** content, respectively), while the isolated yields were almost the same (84–85%) which resulted in high selectivities to **BAB** (82–84%) (Table **2**/Entries 3 and 4).

It can also be observed that the initial rates (v_0) were higher in methanol (2.35 and 3.17 mmol H_2 $mmol_{Pd}^{-1}min^{-1}$) than in toluene (1.66 and 1.91 mmol H_2 $mmol_{Pd}^{-1}$ min^{-1}), due to the different polarities of these solvents.

These results confirm our findings described in Section 2.1., *i.e.* it is favourable to synthesize the Schiff base in warm toluene (50 °C) and to isolate it. On the other hand, it is inexpedient to carry out its hydrogenation in methanol (a protic solvent) due to the considerable hydrogenolytic side-reactions.

2.2.3. Influence of Amount of Catalyst

The influence of different amount of 10% Pd/C (Selcat Q) catalyst on the hydrogenation of **BDAB**, in toluene, is shown in (Table **3**).

As seen, increasing the catalyst/substrate ratio (0.02 → 0.3) was accompanied with decreasing the isolated yield of **BAB** (93 → 83%). Presumably, due to the large adsorption capacity of activated carbon, a small portion of the product, which was directly proportional to the amount of catalyst, remained on the surface of it. In all cases, however, the conversion of **BDAB** was complete, but this required longer reaction time (85 min) using a lower quantity of catalyst (0.02 gg^{-1}) than at 0.3 catalyst/substrate ratio (20 min) (Table **3**/Entries 1 and 5). The purity of product, irre-

spectively of the amount of catalyst, was very high (>96% **BAB** content) in every hydrogenation reaction.

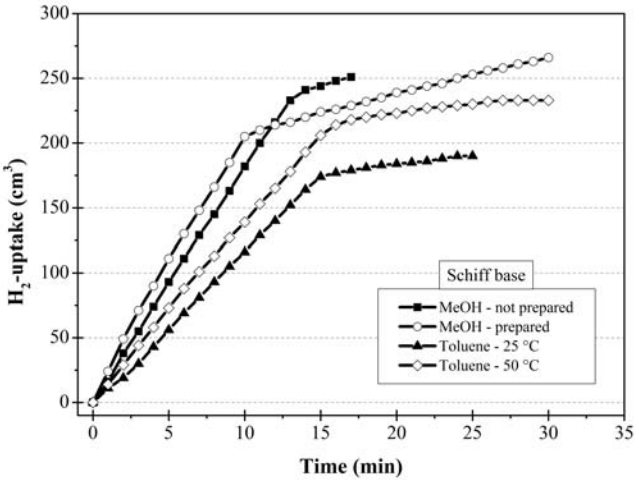


Fig. (1). Hydrogen uptake of **BDAB** prepared in different ways *vs*. time. Conditions: see Table **2**.

Furthermore, the initial rates gradually diminished (4.47 → 1.60 mmol H_2 $mmol_{Pd}^{-1}$ min^{-1}) by increasing the catalyst/substrate ratio which refers to mass transport limitation. This phenomenon often occurs in atmospheric hydrogenations, especially in case of functional groups (*e.g.* NO_2, C=C, C=N) to be hydrogenated easily.

On the basis of our results, it can be stated that applying 0.02 catalyst/substrate ratio is enough to obtain (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol with complete conversion, high purity (~97% **BAB** content), isolated yield (93%) and selectivity (90%), in toluene.

2.2.4. Effect of Solvents

As known [36], in the catalytic hydrogenations both the selectivity of a reaction and the activity of a catalyst can be influenced by using appropriate solvents.

The results of the hydrogenation of **BDAB** in different solvents, over 10% Pd/C (Selcat Q) catalyst are summarized in (Table **4**).

In dichloromethane or ethyl acetate **BAB** was obtained with purity below 94% which is not suitable for optical resolution (Table **4**/Entries 2 and 5). In addition, as seen in (Fig. **2**), the reaction was the slowest in dichloromethane (v_0=1.52 mmol H_2 $mmol_{Pd}^{-1}$ min^{-1}), but the isolated yield (95%) was the highest among solvents tested (Table **4**/Entry 2). In these reductions the ratio of the "favourable" hydrogenolytic steps shown in (Scheme **2**) decreased resulting in more by-product, namely benzyl alcohol was formed in a higher amount (4–5%) and remained in the isolated product, *i.e.* its further hydrogenolysis to toluene was avoided. Since the application of dichloromethane is limited due to its harmful properties, it can be replaced by ethyl acetate without significant decreasing in activity and selectivity. Using toluene or tetrahydrofuran the product was formed with adequate purity (>95%), and the initial rates (v_0) were high (3.04 and 2.56 mmol H_2 $mmol_{Pd}^{-1}$ min^{-1}) (Table **4**/Entries 1 and 3).

In hexane, after reaching about 80% conversion of **BDAB**, the product was precipitated from the reaction mixture. Surprisingly, despite this agglomeration of **BAB**, the reduction took place with practically complete conversion (Table **4**/Entry 4). After filtering the catalyst–product suspension, the precipitated **BAB** was dissolved in toluene and the solvent was evaporated in vacuum which resulted in extremely pure (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (99.5%). Although the isolated yield became significantly lower (72%) than its average value (90%), this loss corresponds with the two crystallization of the crude product.

This "recrystallizing" hydrogenation method, however, may provide new facilities for the liquid-phase, heterogeneous catalytic hydrogenations. Using this technique, the amount of solvents applied can be reduced, and thus the environmental load can be decreased, as well as the apparatus demand can be lower and the operation time can be shorter.

2.2.5. "Recrystallizing" Hydrogenations

The results of the "recrystallizing" hydrogenation of **BDAB** in hexane, over 10% Pd/C (Selcat Q) catalyst are shown in (Table **5**).

At lower catalyst/substrate ratios (0.05 and 0.08) the catalyst was agglomerated by the substrate and this conglomerate separated out onto the wall of reactor, thus the rate of hydrogen uptake was very low. Therefore dichloromethane or toluene were added to the reaction mixture, wich resulted in change of consistency of the reaction mixture, to make easier the course of hydrogenation (Table **5**/Entries 1 and 2). However, the aforementioned product precipitation was observed only at 0.08–0.3 catalyst/substrate ratios, which was accom-

Table 3. Influence of amount of catalyst (10% Pd/C) in the hydrogenation of BDAB.

Entry	Catalyst/substrate Ratio (g g^{-1})	Reaction Time for Complete Conversion (min)	Isolated Yield (%)	BAB Content (%)	Selectivity (%)	v_0 (mmol H_2 $mmol_{Pd}^{-1}$ min^{-1})
1	0.02	85	93	96.9	90	4.47
2	0.05	40	91	96.6	88	3.56
3	0.1	40	88	96.9	86	3.04
4	0.2	30	85	98.9	84	1.91
5	0.3	20	83	96.4	80	1.60

Conditions: 1.70 g Schiff base, 10% Pd/C catalyst (Selcat Q), 30 cm^3 toluene, atmospheric pressure, 25 °C.

Table 4. Effect of solvents in the hydrogenation of BDAB.

Entry	Solvent	Conversion (%)	Isolated Yield (%)	BAB Content (%)	Selectivity (%)	v_0 (mmol H_2 $mmol_{Pd}^{-1}$ min^{-1})
1	toluene	100	88	96.9	86	3.04
2	dichloromethane	98	95	92.8	90	1.52
3	tetrahydrofuran	98	91	95.4	82	2.56
4[a]	hexane	98	72[b]	99.5[b]	73[b]	2.04
5[c]	ethyl acetate	98	94	93.7	90	3.13

Conditions: 1.70 g Schiff base, 0.17 g 10% Pd/C catalyst (Selcat Q), 30 cm^3 solvent, atmospheric pressure, 25 °C, reaction time: 40 min.

[a] Product precipitation.

[b] These values are referred to the precipitated product dissolved by toluene.

[c] Reaction time: 30 min.

panied with decreasing the isolated yield of **BAB** (94 → 72%) (Table **5**/Entries 2-4). In all cases the conversion of **BDAB** was pratically complete, but this required longer reaction time (75 min) using a lower quantity of catalyst (0.05 gg^{-1}) than at 0.3 catalyst/substrate ratio (30 min) (Table **5**/Entries 1 and 4). Furthermore, similarly to toluene (Section 2.2.3.), the purity of product, irrespectively of the amount of catalyst, was also very high (>98% **BAB** content).

Accordingly, in hexane it is favourable to use 0.1 catalyst/substrate ratio of 10% Pd/C to achieve excellent purity of the product (99.5%), near complete conversion and reasonable isolated yield (72%) during the preparation of (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol.

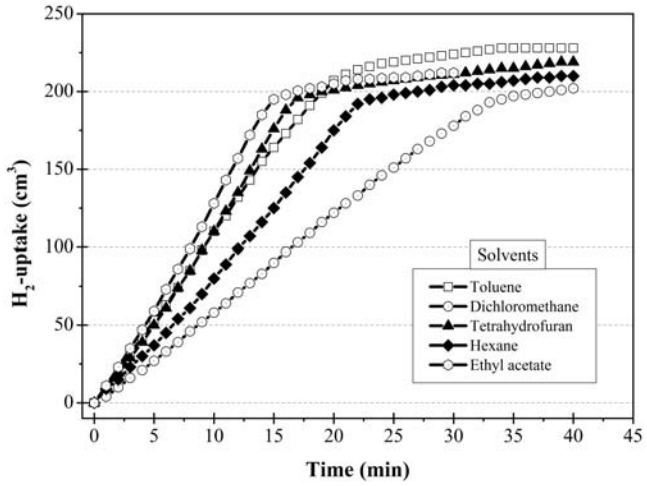


Fig. (2). Hydrogen uptake of **BDAB** *vs*. time in different organic solvents. Conditions: see Table **4**.

3. CONCLUSIONS

An efficient and environmentally benign method for the synthesis of (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (**BAB**) from its Schiff base by palladium mediated, heterogeneous catalytic hydrogenation was developed. We found that it is favourable to synthesize the Schiff base in warm toluene (50 °C) to achieve the highest isolated yield (96%) and purity (98.2%) of (*S*)-(+)-2-(*N*-benzylideneamino)butan-1-ol, as well as it is expedient to carry out its catalytic hydrogenation in an apolar solvent (toluene) to obtain (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol with high purity (>95%) and complete conversion, in a fast reaction.

Applying 10% Pd/C (Selcat Q) catalyst, at 0.02 catalyst/substrate ratio, in toulene, at room temperature and atmospheric pressure **BAB** was isolated with high purity (97%), isolated yield (93%) and selectivity (90%). In this form it can be used as a resolving agent.

Although product precipitation was observed during the hydrogenations carried out in hexane, the reduction took place with neat complete conversion and resulted in extremely pure (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (99.5%), but with lower isolated yield (72%). This "recrystallizing" hydrogenation method, however, may provide new facilities for the liquid-phase, heterogeneous catalytic hydrogenations (lower solvent, apparatus or time demand).

4. EXPERIMENTAL

4.1. Materials

The 10% Pd/C (Selcat Q) catalyst was manufactured in accordance with the patent [37], in the Szilor Fine Chemicals (Budapest, Hungary). The dispersion of the catalyst, determined by H_2-, O_2- and CO-chemisorption measurements, is the following: $D_{10\%\ Pd/C}$=0.50 [38].

Benzaldehyde (>99%) and (*S*)-(+)-2-aminobutan-1-ol (>98%) were supplied by Sigma-Aldrich (Steinheim, Germany), while toluene (p.a.), methanol (p.a.), dichloromethane (p.a.), tetrahydrofuran (p.a.), ethyl acetate (p.a.) and hexane (p.a.) were purchased from Merck-Schuchardt (Dramstadt, Germany).

4.2. Preparation of the Schiff Base

To a solution of (*S*)-(+)-2-aminobutan-1-ol (**AB**) (0.89 g, 10 mmol) in toluene (20 cm^3) was added benzaldehyde (**BA**) (1.06 g, 10 mmol) in toluene (10 cm^3). The mixture was stirred at 50 °C for 10 min. After cooling it was evaporated under vacuum (30 min) to obtain 1.70 g (9.6 mmol) crude product [(*S*)-(+)-2-(*N*-benzylideneamino)butan-1-ol, **BDAB**] with 96% yield, as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (t, *J*=7.4 Hz, 3H, CH_2CH_3), 1.53–1.67 (m, 2H,

Table 5. "Recrystallizing" hydrogenation of BDAB in hexane.

Entry	Catalyst/substrate Ratio (g g^{-1})	Reaction Time (min)	Conversion (%)	Isolated Yield (%)	BAB Content (%)	Selectivity (%)	v_0 (mmol H_2 $mmol_{Pd}^{-1}$ min^{-1})
1[a]	0.05	75	98	94	96.4	90	0.87
2[b,d]	0.08	70	98	61[c]	98.8[c]	62[c]	1.04
3[b]	0.1	40	98	72[c]	99.5[c]	73[c]	2.04
4[b]	0.3	30	99	69[c]	98.6[c]	69[c]	1.60

Conditions: 1.70 g Schiff base, 10% Pd/C catalyst (Selcat Q), 30 cm^3 hexane, atmospheric pressure, 25 °C.

[a] Dichloromethane was added (+ 5 cm^3).

[b] Product precipitation.

[c] These values are referred to the precipitated product dissolved by toluene.

[d] Toluene was added (+ 5 cm^3).

C*H*$_2$CH$_3$), 2.93 (br s, 1H, O*H*), 3.15–3.23 (m, 1H, C*H*), 3.69–3.81 (m, 2H, C*H*$_2$OH), 7.32–7.40 (m, 3H, Ar-*H*), 7.68–7.71 (m, 2H, Ar-*H*), 8.25 (s, 1H, C*H*=N); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.74 (CH_3), 25.04 (CH_2), 66.10 (CH_2OH), 74.60 (CH), 128.36 (2×Ar-CH), 128.60 (2×Ar-CH), 130.79 (Ar-CH), 135.89 (Ar-C), 162.05 (CH=N); GC–MS *m/z* (rel%) 176(8), 146(100), 91(52), 77(15), 41(22), 28(21). Mass spectra (MS) of the starting materials detected by GC are the following: **AB** *m/z* (rel%) 89(1), 58(100), 42(43), 30(33); **BA** *m/z* (rel%) 106(46), 105(47), 77(100), 51(46), 28(58). These analytical results are in agreement with the literary data [17, 39].

4.3. Hydrogenations

The hydrogenation reactions were carried out in a conventional atmospheric pressure apparatus with a magnetic stirrer (stirring speed: 1100 rpm), at room temperature. The initial rates (v_0) were determined from the hydrogen consumption curves.

Typically, the reactor containing **BDAB** (1.70 g), 10% Pd/C catalyst (0.17 g) and toluene (30 cm^3) was flushed with nitrogen and hydrogen, then charged with hydrogen to the specified pressure. After finishing the hydrogen uptake, the catalyst was filtered off and the solvent was removed in vacuum. The amount of the pale yellow, solid, crude product was 1.62 g (91%). After recrystallisation from hexane (*S*)-(+)-2-(*N*-benzylamino)butan-1-ol (**BAB**) was obtained as a white solid. M.p. 71–72 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93 (t, *J*=7.5 Hz, 3H, CH$_2$C*H*$_3$), 1.46–1.57 (m, 2H, C*H*$_2$CH$_3$), 1.89 (br s, 2H, N*H* and O*H*), 2.62–2.66 (m, 1H, C*H*), 3.34 (dd, *J*=10.6, 6.3 Hz, 1H, C*H*HOH), 3.66 (dd, *J*=10.6, 3.8 Hz, 1H, CH*H*OH), 3.81 (dd, *J*=12.9, 9.0 Hz, 2H, PhC*H*$_2$), 7.26–7.34 (m, 5H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.58 (CH_3), 24.52 (CH_2), 51.21 ($PhCH_2$), 59.94 (CH), 62.73 (CH_2OH), 127.35 (Ar-CH), 128.33 (2×Ar-CH), 128.72 (2×Ar-CH), 140.51 (Ar-C); GC–MS *m/z* (rel%) 178(1), 148(30), 91(100), 70(12), 65(18); $[\alpha]_D^{20} = +23.3$ (*c* 0.9, EtOH); lit. $[\alpha]_D^{20} = +28.0$ (*c* 1.2, $CHCl_3$) [22]. Mass spectra (MS) of the by-products formed in lower amounts and detected by GC are the following: (*S*)-(+)-2-(*N,N*-dibenzylamino)butan-1-ol (**DBAB**) *m/z* (rel%) 268(1), 238 (25), 190(8), 146(5), 91(100), 65(12); benzyl alcohol (**BnOH**) *m/z* (rel%) 108(40), 91(12), 79(100), 77(60), 51(21) 39(11). These analytical results are in agreement with the literary data [39].

Every hydrogenation was reproduced 2–3 times, and the average value of the results was given. The deviation was less than 5%.

4.4. Analysis

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-300 spectrometer operating at 300 and 75 MHz, respectively, in chloroform-D1 ($CDCl_3$). Chemical shifts are given relative to δ_{TMS}.

GC analyses were carried out with a Thermo Finnigan Focus GC apparatus using a Supelco β-DEX^{TM} 120 capillary column (30 m × 0.25 mm ID, 0.25 μm film) FID. The temperature program was the following: 90 °C (4 min) to 210 °C at 10 °C/min and hold 5 min, then to 220 °C at 10 °C/min, hold 5 min.

GC–MS analyses were carried out with a Finnigan Mat/Automass II GC/MS spectrometer using a Zebron ZB-5ms capillary column (30 m × 0.25 mm ID, 0.25 μm film). The temperature program was the following: 45 °C (2 min) to 300 °C at 10 °C/min, then to 350 °C at 25 °C/min.

Melting points were taken using a MEL-TEMP® apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter.

Selectivity values to **BAB** were calculated according to the following equation:

$$\text{Selectivity (\%)} = \frac{\text{isolated yield x } \mathbf{BAB} \text{ content}}{\text{conversion}} \text{ x } 100$$

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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