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Hydrogenolysis of *N*-protected aminooxetanes over palladium: An efficient method for a one-step ring opening and debenzylation reaction

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ABSTRACT

An efficient method for the palladium mediated hydrogenation of an optically active, *N*-protected aminooxetane derivative has been developed. Using appropriate solvents, in a one-step reaction, a chiral 1,4-aminoalcohol derivative [(2*S*,3*R*)-4-amino-3-benzoyloxy-2-benzylbutan-1-ol] was formed over a Pd/C catalyst, during hydrogenolytic ring opening and debenzylation reactions.

1. Introduction

Chiral 1,4-aminoalcohols can be useful intermediates for the synthesis of biologically active *N*-heterocycles. Ring closuring reaction between the amino and hydroxyl groups, under the Mitsunobu protocol [1], is an alternative route to produce non-racemic pyrrolidines. There are several protein kinase C enzyme inhibitors among the optically active, 3,4-disubstituted pyrrolidines used in the treatment of certain cancer diseases [2]. Previously we reported a method, in which aminooxetanes could stereoselectively be obtained from chiral disubstituted oxiranes in the presence of potassium *tert*-butoxide activated lithium diisopropylamide (LiDA–KOR) [3]. Furthermore, pure enantiomers of 3-[1′-hydroxy-2′-(dibenzylamino)ethyl]-2-phenyloxetane were synthesized from *cis*-4-benzyloxy-2,3-epoxybutanol using enzymatic kinetic resolution followed by consecutive tosylation, dibenzylamination and organometallic base promoted enantioselective rearrangement reactions [4]. Recently we have developed an efficient, one-step process for the palladium mediated hydrogenation of an optically active, *O*-trityl hydroxyoxetane derivative, in which chiral 1,4-diol was formed over a Pd/C catalyst, in a dichloromethane/methanol solvent mixture (1:4), during hydrogenolytic ring opening and detritylation reactions [5].

In this work, adopting the aforementioned hydrogenation method, the heterogeneous catalytic hydrogenolysis of (−)-(2*S*,3*S*,1′*S*)-3-[1′-benzoyloxy-2′-(dibenzylamino)ethyl]-2-phenyloxetane (**1**) to (2*S*,3*R*)-4-amino-3-benzoyloxy-2-benzylbutan-1-ol (**2**) was investigated in detail (Scheme 1). Compound **2** is a potential starting material for preparing optically active, practically important pyrrolidine derivatives.

Since the hydrogenolysis of **1** has never been described in the literature, the ring opening methods of oxetanes and the benzyl group removing procedures, respectively, are shown through other examples.

To open an oxetane ring the common methods are applying acidic conditions, such as H_2SO_4 in methanol [6], CF_3COOH in dichloromethane [7], ethereal H_2O_2 in the presence of $Yb(OTf)_3$ [8] or benzoyl chloride with SmI_2 in tetrahydropyran [9]. Few examples have been reported on the hydrogenolysis of oxetanes. Thus, 1,2-diols were prepared via hydrogenolysis of 2-aryl-3-(silyloxy)oxetanes over Pd(0) catalysts (e.g. Pd/C), but the acid sensitive silyloxy group remained intact if $Pd(OH)_2$ was applied as a catalyst for the hydrogenolysis [10]. Oxetane ring containing cycloadducts of 3,4-dihydro-2(1H)-pyridinone derivatives were transformed into 2-arylmethyl-3-piperidinols by hydrogenolysis of the oxetane ring, in methanol, over $Pd(OH)_2$ [11]. Other cyclic ethers, 2-phenyltetrahydropyran or phenyldioxane, were hydrogenated to the corresponding alcohols with 72–75% yields, over a 5% Pd/C catalyst, in acetic acid, in the presence of $HClO_4$ or H_2SO_4, at 3 bar and room temperature [12], i.e.

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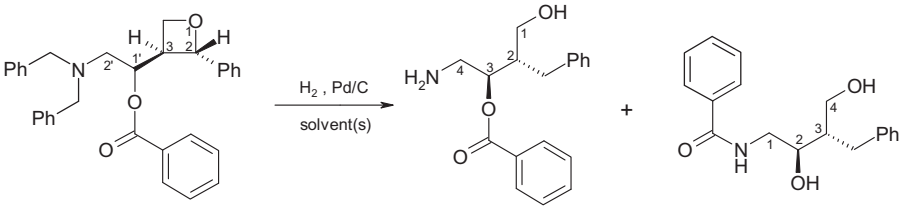


Scheme 1. Hydrogenolysis of (−)-(2*S*,3*S*,1′*S*)-3-[1′-benzoyloxy-2′-(dibenzylamino)ethyl]-2-phenyloxetane (**1**).

these hydrogenolytic reactions took place under strong acidic conditions.

As well known, debenzylation is a common method to obtain the active forms of amines or alcohols from the corresponding *N*- or *O*-protected derivatives [13,14]. Among the typical hydrogenation catalysts, such as platinum metals, nickel or copper chromite, palladium is by far the most favoured one due to its high activity and selectivity [15]. Removing the benzyl group attached to nitrogen, however, does not readily take place as its cleavage from oxygen does [16,17]. The ease of *N*-debenzylation is influenced by substitution on the nitrogen atom [18], namely the quaternary and tertiary amines can easily be debenzylated already at atmospheric pressure and room temperature, while that of the secondary or primary ones require higher pressure (>4 bar) and temperature (>40 °C). Moreover, the products of hydrogenolysis are strongly basic amines which can deactivate the supported precious metal catalysts due to their poisoning effects [19–21], therefore a higher amount of catalyst or adding acids are necessary to complete the reaction.

In this paper the effects of solvents and catalyst/substrate ratio on the hydrogenation of **1** and the selectivity to **2** are discussed.

2. Experimental

2.1. Materials

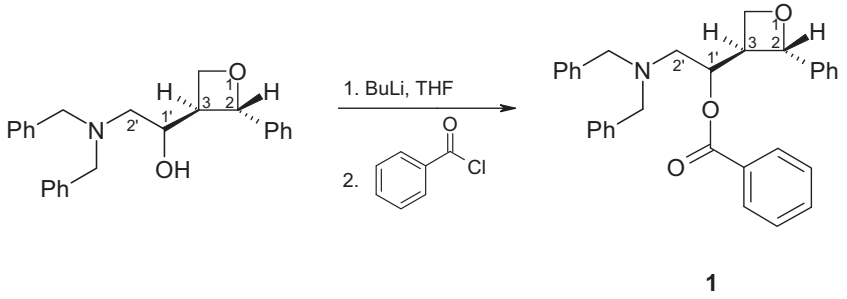
The 10% Pd/C (Selcat Q) catalyst was manufactured in accordance with the patent [22], in the Szilor Fine Chemicals (Budapest, Hungary). The dispersion of the catalyst, determined by H_2-, O_2- and CO-chemisorption measurements, is $D = 0.50$ [23].

Methanol (p.a.) and tetrahydrofuran (p.a.) were supplied by Merck-Schuchardt (Hohenbrunn, Germany), while dichloromethane (p.a.) were purchased from Reanal Fine Chemicals (Budapest, Hungary).

Synthesis of compound **1** (Scheme 2): a solution of (−)-(2*S*, 3*S*,1′*S*)-3-[1′-hydroxy-2′-(dibenzylamino)ethyl]-2-phenyloxetane, prepared according to our procedure described in [4], (3.0 g, 8.03 mmol) in THF (40 mL) was cooled to −75 °C under nitrogen atmosphere, then buthyllithium in hexane (5.1 mL, 8.03 mmol) was added to the mixture and it was stirred for 40 min. After adding benzoyl chloride (0.93 mL, 8.03 mmol), the reaction mixture was stirred for 40 min again, then it was warmed up to room temperature and stirred overnight. Afterwards it was diluted with diethyl ether (60 mL), distilled water (30 mL) and saturated sodium hydrogen carbonate solution (30 mL) and the two phases formed were separated. The aqueous phase was extracted with diethyl ether (3×50 mL) and the combined ethereal extracts were washed with saturated sodium hydrogen carbonate solution (3×50 mL) and brine (2×50 mL), then dried over Na_2SO_4. After evaporating the solvent, 3.52 g crude product was obtained. It was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 4:1) to give 3.11 g yellowish oil of **1** (81%). ^{1}H NMR ($CDCl_3$, 500 MHz), δ ppm 2.44 (1H, dd, $J = 4.5$, 14.0 Hz, NCH_aH_b), 2.71 (1H, dd, $J = 7.5$, 15.0 Hz, NCH_aH_b), 3.14 (1H, m, oxetane CH), 3.43 (2H, d, $J = 13.5$ Hz, NCH_2Ph), 3.73 (2H, d, $J = 13.5$ Hz, NCH_2Ph), 4.49 (1H, t, $J = 6.5$ Hz, oxetane CH_2O), 4.55 (1H, t, $J = 6.5$ Hz, oxetane CH_2O), 5.62 (1H, d, $J = 6.5$ Hz, oxetane C*H*Ph), 5.81 (1H, m, C*H*OCOPh), 7.20–7.31 (17H, m, Ar–CH), 7.45 (2H, t, $J = 8.0$ Hz, benzoyl *m*-Ph), 7.57 (1H, t, $J = 8.0$ Hz, benzoyl *p*-Ph), 8.01 (2H, d, $J = 8.0$ Hz, benzoyl *o*-Ph); ^{13}C-NMR ($CDCl_3$, 75 MHz), δ ppm 47.0, 55.5, 69.8, 72.5, 85.4, 96.4, 125.6, 127.3, 128.1, 128.6, 128.7, 129.2, 130.1, 130.2, 130.8, 133.4, 139.0, 142.5, 166.4. $[\alpha]_D^{20} = -7.2$, (*c* 1.65, $CHCl_3$), ee 93%.

2.2. Hydrogenations

The hydrogenation reactions were carried out either in a conventional atmospheric pressure apparatus with a magnetic stirrer (stirring speed: 1100 rpm) or in a 250 cm^3 stainless steel autoclave (Technoclave, Budapest, Hungary) equipped with a magnetic stirrer (stirring speed: 1100 rpm), at 10 bar hydrogen pressure and room temperature. The reactor containing the starting material, catalyst and solvent was flushed with nitrogen and hydrogen, then charged with hydrogen to the specified pressure. The reaction was followed by TLC (*n*-hexane/ethyl acetate = 4:1; R_f (**1**) = 0.50, and dichloromethane/methanol = 5:1; R_f (**2**) = 0.46, R_f (**3**) = 0.91). After the hydrogenation was completed, the catalyst was filtered off and the solvent was removed in vacuum. The residue was purified by column chromatography on sil-



Scheme 2. Synthesis of (−)-(2*S*,3*S*,1′*S*)-3-[1′-benzoyloxy-2′-(dibenzylamino)ethyl]-2-phenyloxetane (**1**).

Table 1
Hydrogenolysis of **1** in different solvents.[a]

No.	Solvents	Pressure (bar)	Reaction time (h)	Conversion of **1** (%)	Isolated yield (%)	
					Compound **2**	Compound **3**
1	Methanol	1	4.0	100	0	20
			72.0	100	0	52
2	Tetrahydrofuran	1	5.0	0	–	–
		10	24.0	0	–	–
3	Dichloromethane	1	5.0	0	–	–
		10	12.0	0	–	–
4[b]	Dichloromethane	10	12.0	100	57[c]	0[d]
			24.0	100	70[c]	0[d]

[a] Conditions: 0.3 g (0.63 mmol) substrate, 0.15 g 10% Pd/C catalyst (Selcat Q), 30 mL solvent, 30 °C.
[b] 45 °C.
[c] Prepared in a form of **2**.HCl salt.
[d] No formation of compound **3** was observed.

ica gel (dichloromethane/methanol = 5:1). Representative physical and spectroscopic data of the products are the following:

(2*S*,3*R*)-4-Amino-2-benzyl-3-benzoyloxybutan-1-ol (**2**), oil, ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 2.39–2.54 (2H, m, CH_aH_bPh and $CHCH_2OH$), 2.78 (1H, dd, J = 4.2, 13.5 Hz, CH_aH_bPh), 3.30 (1H, m, CH_2NH_2), 3.37 (1H, dd, J = 4.5, 14.4 Hz, CH_2NH_2), 3.47 (1H, m, CH_aH_b–OH), 3.62 (1H, dd, J = 2.4, 11.7 Hz, CH_aH_b–OH), 5.51 (1H, m, CHOCOPh), 7.12–7.34, (7H, m, Ar–CH), 7.47 (1H, t, J = 7.5 Hz benzoyl *p*-Ph), 8.01 (2H, d, J = 7.5 Hz, benzoyl *o*-Ph); ^{13}C NMR ($CDCl_3$, 125 MHz) δ ppm 33.5, 42.0, 44.5, 60.1, 72.4, 126.6, 128.6, 128.7, 129.3, 129.4, 133.6, 139.0, 166.8; ν_{max} (film, cm^{-1}) 3301, 2936, 1633, 1536, 1038, 695. $[\alpha]_D^{20} = 0$ (*c* 1.55, $CHCl_3$), ee 93%.

(2*R*,3*S*)-*N*-(3-Benzyl-2,4-dihydroxybutyl)benzamide (**3**), white crystal, m.p. 153 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 1.92 (1H, m, $CHCH_2$Ph), 2.58 (1H, m, CH_aH_bPh), 2.92 (1H, m, CH_aH_bPh), 3.55 (2H, m, CH_2OH), 3.74 (1H, m, CH_aH_bNH), 3.90 (1H, m, CH_aH_bNH), 4.00 (1H, m, CHOH), 7.10–8.20 (10H, m, Ar–CH).

2.3. Synthesis of (–)-(3R,4S)-3-benzoyloxy-4-benzylpyrrolidine (*5*)

(2*S*,3*R*)-4-Amino-3-benzoyloxy-2-benzylbutan-1-ol (**2**, 2.6 mmol, 0.8 g) was dissolved in tetrahydrofuran (25 mL) and the solution was cooled down to 0 °C. Triphenylphosphine (2.6 mmol, 0.68 g) and diethyl azodicarboxylate (2.6 mmol, 1.13 g) was added, then the mixture was stirred for an hour at 0 °C and 48 h at 25 °C. The solvent was evaporated in vacuum and the crude product (2.2 g) was purified by column chromatography (eluent: dichloromethane/metanol = 10:1) to give (–)-(3*R*,4*S*)-3-benzoyloxy-4-benzylpyrrolidine (**5**) as an oil (0.56 g, 75%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 2.86 (1H, dd, J = 4.8, 12.3 Hz, $PhCH_aH_b$), 3.04 (1H, dd, J = 4.8, 12.3 Hz, $PhCH_aH_b$), 3.17 (2H, m, $BnCHCH_2$), 3.54 (2H, m, $OCHCH_2$), 3.76 (1H, m, BnCH), 5.32 (1H, m, CHOCOPh), 7.23–7.37 (5H, m, Ar–CH), 7.49 (2H, t, J = 7.8 Hz benzoyl *m*-Ph), 7.60 (1H, t, J = 7.8 Hz, benzoyl *p*-Ph), 8.07 (2H, d, J = 7.8 Hz, benzoyl *o*-Ph); ^{13}C NMR (DMSO-d_6, 75 MHz) δ ppm 35.5, 44.9, 47.6, 48.8, 126.4, 128.5, 128.6, 128.8, 129.1, 129.4, 133.6, 138.7, 165.0; ν_{max} (KBr, as oxalate salt, cm^{-1}) 3434, 2925, 1720, 1632, 1277, 720. $[\alpha]_D^{20} = -26.9$ (*c* 2.05, $CHCl_3$), ee 93%.

2.4. Analysis

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 or DRX-300 spectrometers operating at 500 or 300 and 125 or 75 MHz, respectively, in chloroform-D1 ($CDCl_3$) or in dimethyl sulfoxide (DMSO-d_6). Chemical shifts are given relative to δ_{TMS}. IR spectra were taken on a Perkin-Elmer 1600 FT spectrometer. Optical rotations were measured with a Perkin-Elmer 241 automatic polarimeter. TLC was carried out on Kieselgel 60 F_{254} (Merck) sheets.

3. Result and discussion

3.1. Effect of solvents

As known [24], 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 hydrogenolysis of **1** in different organic solvents, over 10% Pd/C (Selcat Q) catalyst are summarized in Table 1.

In methanol, the conversion of compound **1** was complete at atmospheric pressure and 30 °C after 4 h reaction time, but the wanted compound **2** was not formed. Surprisingly a side-product, (2*R*,3*S*)-*N*-(3-benzyl-2,4-dihydroxybutyl)benzamide (**3**), was isolated from the reaction mixture with 20% yield. Further hydrogenation of **1**, after 72 h, also provided compound **3** with higher isolated yield (52%). It means that after opening the oxetane ring, the two benzyl groups were removed already at atmospheric pressure and room temperature, but hydrogenolysis of secondary amines, in general, requires higher pressure (>4 bar) and temperature (>40 °C) [18]. This unexpected result will be discussed later.

Using tetrahydrofuran or dichloromethane no conversion of **1** was observed even after 12–24 h reaction time and at 10 bar and 30 °C. In dichloromethane, however, compound **2** was obtained with 57% yield, when the temperature was raised to 45 °C, but it was isolated in a form of hydrogen chloride salt (**2**.HCl). Further hydrogenation of **1** at 10 bar and 45 °C, after 24 h, provided compound **2**.HCl with 70% yield, moreover no compound **3** was detected. This was due to the hydrodehalogenating ability of palladium [25], i.e. under such conditions palladium is able to hydrogenolyse dichloromethane, and the hydrogen chloride formed gives a salt with compound **2**.

To avoid the unwanted side-reactions, a mixture of dichloromethane and methanol was applied in the hydrogenation of **1**, similarly to our previous results concerning the hydrogenolysis of *O*-protected hydroxyoxetanes [5]. The effect of solvent mixtures with different composition on the conversion of **1** and the isolated yield of **2** is given in Table 2.

As seen, in the 50:50 (v/v%) dichloromethane/methanol mixture compound **2** was isolated with 50% yield (by complete conversion of **1**), over palladium on carbon, at 10 bar and 30 °C, after 4 h reaction time. Similarly to dichloromethane used by itself, no formation of compound **3** was observed, but compound **2** was in a form of free base. Using a 80:20 (v/v%) mixture the complete conversion of **1** required longer reaction time (20 h), moreover the isolated yield of **2** became slightly better (50 → 54%). Whereas, increasing

Table 2
Hydrogenolysis of **1** in the mixture of dichloromethane (CH_2Cl_2) and methanol (MeOH).[a]

No.	CH_2Cl_2/MeOH (v/v %)	Reaction time for complete conversion of **1** (h)	Isolated yield of compound **2**[b] (%)
1	50:50	4.0	50
2	80:20	20.0	54
3	70:30	16.0	79
4[c]	70:30	16.0	87

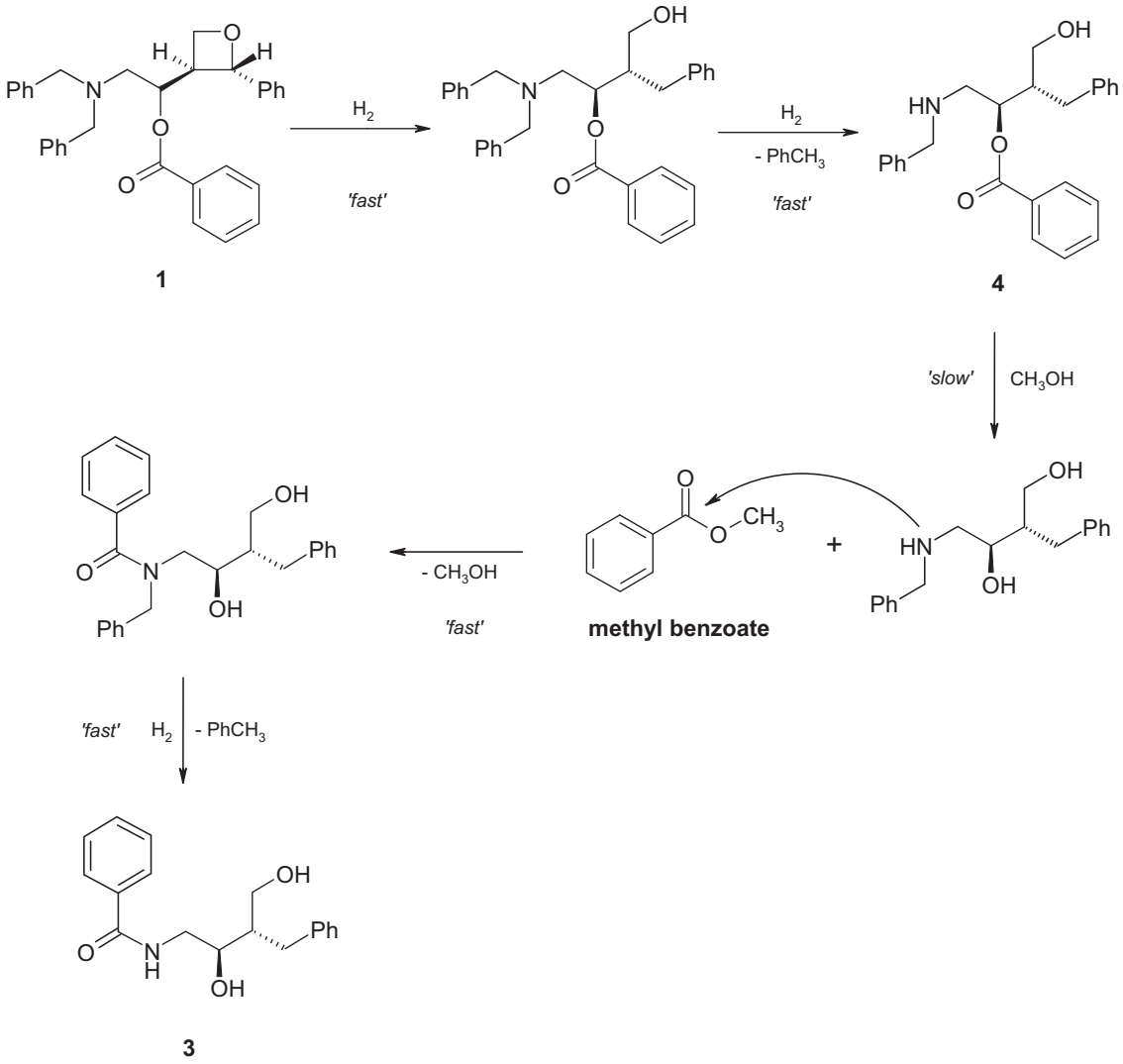
[a] Conditions: 0.3 g (0.63 mmol) substrate, 0.15 g 10% Pd/C catalyst (Selcat Q), 30 mL solvent, 30 °C, 10 bar.
[b] No formation of compound **3** was observed.
[c] 2.85 g (5.98 mmol) substrate, 1.42 g 10% Pd/C catalyst (Selcat Q), 50 mL solvent.

Table 3
Influence of amount of catalyst (Pd/C) in the hydrogenolysis of **1**.[a]

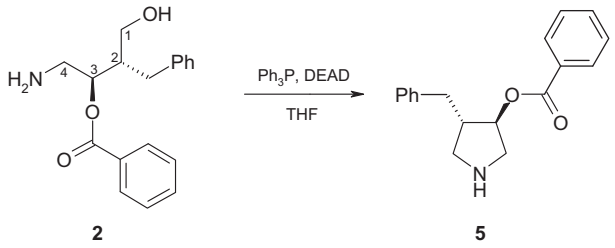
No.	Catalyst/substrate ratio ($g\,g^{-1}$)	Reaction time (h)	Conversion (%)	Isolated yield of compound **2**[b] (%)
1	0.5	16.0	100	79
2	0.3	24.0	32	25
3	0.1	24.0	1	–

[a] Conditions: 0.3 g (0.63 mmol) substrate, 10% Pd/C catalyst (Selcat Q), 21 mL dichloromethane and 9 mL methanol (70:30 v/v %), 30 °C, 10 bar.
[b] No formation of compound **3** was observed.

the amount of methanol to 30 (v/v%) the rate of hydrogenolysis also increased, namely 16 h reaction time was sufficient to complete the hydrogenation of **1**, as well as compound **2** was achieved with 79% isolated yield. Further increase in isolated yield of **2** was obtained (87%), when this reaction was repeated using about ten times higher amount of starting material (0.3 → 2.85 g), presumably due to the smaller loss of **2** suffered during the working-up procedure.



Scheme 3. Proposed mechanism of the formation of compound **3**.



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Scheme 4. Synthesis of (−)-(3*R*,4*S*)-3-benzoyloxy-4-benzylpyrrolidine (**5**).

According to our results, it can be stated that methanol, similarly to other protic and polar solvents, is very efficient in the hydrogenolysis of oxetane ring and the removal of benzyl protecting group, as well as provides high reaction rate, while dichloromethane prevents the possibility of side-reactions (e.g. hydrolysis of the ester bond).

3.2. Influence of amount of catalyst

The results of hydrogenolysis of 1 over different amount of 10% Pd/C (Selcat Q) catalyst, in a 70:30 (v/v%) dichloromethane/methanol solvent mixture are summarized in Table 3.

As seen, the hydrogenation of 1, at 0.5 catalyst/substrate ratio, was complete after 16.0 h reaction time and compound **2** was obtained with 79% isolated yield. At lower catalyst/substrate ratio (0.3) the conversion of 1 was only 32% after 24 h, but the isolated yield of **2** (25%) was proportional with that of the previous experiment. Further decreasing the catalyst/substrate ratio to 0.1 resulted in practically no conversion of **1** even after 24 h, presumably, due to complete poisoning of the palladium catalyst used.

These results indicate that the hydrogenolysis of **1** requires a relatively high catalyst/substrate ratio (0.5) to complete the reaction, probably, due to poisoning effect of the strongly basic nitrogen of these amino compounds.

3.3. Possible reaction mechanism for the formation of side-product **3**

To explain the formation of side-product benzamide derivative (**3**) we suggested the following mechanism shown in Scheme 3. First, the oxetane ring was opened and a benzyl group was removed by the cleavage of carbon–nitrogen bond in a fast reaction step. Then methanol, which was present as a solvent in large excess, could initiate transesterification of the benzoyl ester moiety of **4** in a slow reaction to form methyl benzoate, which could acylate fast the secondary *N*-monobenzyl aminodiol derivative. Since this *N*-benzoyl-*N*-benzyl aminodiol became a tertiary amine again, the hydrogenolysis of benzyl group could take place already at atmospheric pressure and room temperature, over palladium. The appearance of methyl benzoate (M_{rel} = 136.15 g mol^{-1}) was proved by GC–MS measurements. The MS data are the following: *m/z* (rel%) 136 (39), 105 (100), 77 (63), 51 (26), which are in agreement with the literary data [26]. This analytical result gives an indirect evidence of the proposed mechanism.

3.4. Practical importance of product **2**

In order to demonstrate the practical usefulness of the prepared 1,4-aminoalcohol derivative **2**, a ring closure reaction was carried out using the Mitsunobu conditions. Product **5** was isolated in pure form (Scheme 4) which can be used as a key intermediate in the synthesis of Balanol analogues [27].

It has to be emphasized, these chemical transformations have no influence on the configurations of the stereogenic carbon atoms, therefore, starting from optically active **1**, the products (**2** and **5**) were obtained with the same ee.

4. Conclusions

Efficient, selective methods for the palladium mediated hydrogenation of an optically active, *N*-protected aminooxetane derivative (**1**) have been developed. In a one-step reaction chiral 1,4-aminoalcohol (**2**) was formed over a Pd/C catalyst, during a hydrogenolytic ring opening reaction followed by debenzylation. The selectivity and the yield of compound **2** were improved by appropriate solvents. In a dichloromethane/methanol solvent mixture (7:3) the isolated yield of **2** increased to 87%. These results gave further evidences that selectivity, yield and rate of the catalytic hydrogenation reactions can be influenced by changing solvents or solvent mixtures.

In methanol, due to the transesterification of *O*-benzoyl group, a benzamide type by-product (**3**) was formed already at atmospheric pressure and room temperature, because *N*-acetylation made easier the *N*-debenzylation in consequence of a tertiary amine derivative formed.

The synthesized chiral 1,4-aminoalcohol (**2**) can be a promising starting material for synthesis of optically active, valuable and important pyrrolidine derivatives, like compound **5**.

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References

[1] O. Mitsunobu, Synthesis (1981) 1.
[2] V. Pande, M.J. Ramos, F. Gago, Anti-Cancer Agents Med. Chem. 8 (2008) 638.
[3] A. Thurner, F. Faigl, L. Tőke, A. Mordini, M. Vallachi, G. Reginato, G. Czira, Tetrahedron 57 (2001) 8173.
[4] F. Faigl, A. Thurner, M. Battancs, F. Farkas, L. Poppe, V. Bódai, I. Kmecz, B. Simándi, Tetrahedron: Asymmetry 16 (2005) 3841.
[5] F. Farkas, A. Thurner, E. Kovács, F. Faigl, L. Hegedűs, Catal. Commun. 10 (2009) 635.
[6] A. Balsamo, P. Crotti, M. Ferretti, F. Macchia, J. Org. Chem. 40 (1975) 2870.
[7] Th. Bach, J. Schröder, Tetrahedron Lett. 38 (1997) 3707.
[8] P.H. Dussault, T.K. Trullinger, F. Noor-e-Ain, Org. Lett. 4 (2002) 4591.
[9] D.W. Kwon, Y.H. Kim, K. Lee, J. Org. Chem. 67 (2002) 9488.
[10] Th. Bach, Liebigs Ann. 6 (1995) 1045.
[11] Th. Bach, H. Bergmann, H. Brummerhop, W. Lewis, K. Harms, Chem. Eur. J. 7 (2001) 4512.
[12] R.H. Baker, K.H. Cornell, M.J. Cron, J. Am. Chem. Soc. 70 (1948) 1490.
[13] P.N. Rylander, Catalytic Hydrogenation over Platinum Metals, Academic Press, New York, 1967, p449.
[14] M. Freifelder, Practical Catalytic Hydrogenation, Wiley, New York, 1971, p398.
[15] P.N. Rylander, D.R. Steele, Engelhard Ind. Tech. Bull. 6 (1965) 41.
[16] L. Birkofer, Berichte 75 (1942) 429.
[17] R. Baltzly, J.S. Buck, J. Am. Chem. Soc. 65 (1943) 1984.
[18] R. Baltzly, P.B. Russell, J. Am. Chem. Soc. 75 (1953) 5598.
[19] E.B. Maxted, M.S. Briggs, J. Chem. Soc. (1957) 3844.
[20] L. Hegedűs, T. Máthé, Appl. Catal. A 226 (2002) 319.
[21] L. Hegedűs, Magy. Kém. Folyóirat 113 (2007) 139.
[22] T. Máthé, A. Tungler, J. Petró, US Patent 4,361,500 (1982).
[23] A. Sárkány, unpublished results.
[24] P.N. Rylander, in: W.H. Jones (Ed.), Catalysis in Organic Syntheses, Academic Press, New York, 1980, p155.
[25] P.N. Rylander, Catalytic Hydrogenation in Organic Syntheses, Academic Press, New York, 1979, p235.
[26] P.J. Linstrom, W.G. Mallard (Eds.), NIST Chemistry WebBook, NIST Stand.Ref Database No. 69, National Institute of Standards and Technology, Gaithersburg, MD, 2010; http://webbook.nist.gov/chemistry.
[27] J.M. Defauw, M.M. Murphy, G.E. Jagdmann, H. Hu, J.W. Lampe, S.P. Hollinshead, T.J. Mitchell, H.M. Crane, J.M. Heerding, J.S. Mendoza, J.E. Davis, J.W. Darges, F.R. Hubbard, S.E. Hall, J. Med. Chem. 39 (1996) 5215.