Tetrahedron: *Asymmetry* 22 (2011) 351–355

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Enantioselective Henry reaction catalyzed by copper(II)—*Cinchona* alkaloid complexes

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ARTICLE INFO

Article history:
Received 5 January 2011
Accepted 3 February 2011
Available online 1 March 2011

ABSTRACT

An enantioselective Henry reaction was efficiently carried out under mild reaction conditions in the presence of catalytic 9-*epi* and natural *Cinchona* alkaloids and copper (II) acetate. The best catalytic performance was observed for native quinine (12 mol %) and $Cu(OAc)_2$ (10 mol %). Aromatic and aliphatic aldehydes with nitromethane and its α-substituted derivatives provided the corresponding β-nitroalcohols in good to reasonable yields, high *syn*-diastereoselectivity, and (*S*)-enantioselectivity of up to 94% ee.

1. Introduction

Asymmetric Henry (nitroaldol) and aza-Henry reactions offer a simple route to chiral β-nitroalcohols and β-nitroamines, important synthetic intermediates, which are easily transformed into various difunctionalized derivatives and precursors of biologically active compounds.[1] For this reason much effort has been devoted to the development of metal-catalyzed and organocatalytic versions of this reaction.[2,3] The effective catalytic process requires both a Brønsted base (to deprotonate the nitro-compound) and a Lewis acid (to activate the carbonyl group). With respect to this, copper complexes of chiral amines[2g,4] were successfully applied as catalysts, giving the corresponding β-nitroalcohols with high ee. Derivatives of *Cinchona* alkaloids (cinchonine, cinchonidine, quinine, and quinidine, Fig. 1) have already been tested in both Henry and aza-Henry reactions.[5] The direct organocatalytic application of natural *Cinchona* alkaloids in asymmetric nitroaldol reactions requires high pressure conditions and only gave moderate selectivities.[5a,b] However, in 2005, Jørgensen et al. reported an elegant highly stereoselective aza-Henry reaction using *Cinchona* alkaloids as a chiral Brønsted base in combination with a copper(II) chiral bisoxazoline complex as a chiral Lewis acid. The diastereoselectivity was controlled by quinine, while the configuration of the main product was determined by the Lewis acid ligand.[5c] When C-9-*epi*-thioles derived from *Cinchona* alkaloids were tested as chiral ligands in the Cu-catalyzed asymmetric Henry reaction, the process went smoothly with an enantioselectivity of up to 83%.[2k] All these results encouraged us to study the use of natural *Cinchona* alkaloids in the direct Henry reaction carried out in the presence of copper(II) acetate.

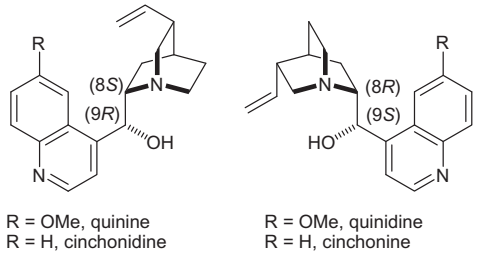
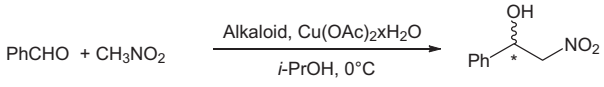


Figure 1.

2. Results and discussion

We examined the catalytic performance of the alkaloids in a model nitroaldol reaction between benzaldehyde and nitromethane. The reaction was carried out in the presence of 12 mol % of alkaloid and 10 mol % of hydrated copper acetate (Scheme 1).



Scheme 1.

The results of the preliminary screening are summarized in Table 1. Thus, all the alkaloids of the 9-native configuration catalyzed the enantioselective reaction giving nitroaldol in good yield. The alkaloid with an (8*R*)-configuration, gave mainly the (*R*)-product while those with an (8*S*)-configuration produced mostly the (*S*)-isomer. We also tested other solvents (dichloromethane, acetonitrile, ethanol, etc.) and *i*-PrOH was chosen as the most suitable one. The standard reaction performed with

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doi:10.1016/j.tetasy.2011.02.003

quinine at −20 °C gave less yield (53%) and 81% ee. When quinine was used in the absence of copper acetate (entry 8), a very small excess of the (*R*)-product was obtained. Furthermore, the 9-*epi* alkaloids (entries 6 and 7) led to nearly negligible enantioselectivities. An almost racemic product was obtained using quinine with $Zn(OAc)_2$, $Co(OAc)_2$ or $VO(OAc)_2$, but when a system of quinine (12 mol %) and Et_2Zn (10 mol %) was applied in toluene at −20 °C for 3 days, a 94% yield of the nitroaldol with 19% ee (*R*) resulted. Furthermore, the results in Table 1 show that 6'-methoxy alkaloids (quinidine and quinine, entries 3 and 4) performed better than the unsubstituted ones (cinchonidine and cinchonine, entries 1 and 2). We have already observed the same tendency with the 9-*epi*-thioles of quinine and other alkaloids, where it could be ascribed to the formation of an additional hydrogen bond, thus stabilizing the corresponding transition state of the similar copper-catalyzed Henry reaction.[2k] The same interaction may operate here; however, an important difference between these catalysts should be noted. Thus, the 9-*epi*-HS-alkaloids gave much higher ee's than their epimers (e.g., 9-*epi*-HS-quinine gave 83% ee, while 9-HS-quinine gave 14% ee only)[2k] and quite the opposite tendency is observed here (Table 1, entries 4 vs 6 and 3 vs 7). The stereochemical sense of induction for both types of catalysts was the same, that is, the configuration of the product is tied to the configuration at the C-8 center of the alkaloid.

Table 1
Nitroaldol reaction of nitromethane and benzaldehyde catalyzed by alkaloid/$Cu(OAc)_2$[a]

Entry	Ligand	Yield (%)	ee [b](%)	Absolute configuration[c]
1	(8*S*,9*R*)-Cinchonidine	42	53	(*S*)
2	(8*R*,9*S*)-Cinchonine	55	47	(*R*)
3	(8*R*,9*S*)-Quinidine	73	59	(*R*)
4	(8*S*,9*R*)-Quinine	87	86	(*S*)
5	(8*S*, 9*R*)-DHQN	84	58	(*S*)
6	(8*S*,9*S*)-*epi*-Quinine	61	2	(*S*)
7	(8*R*,9*R*)-*epi*-Quinidine	38	7	(*R*)
8	(8*S*,9*R*)-Quinine without $Cu(OAc)_2{\cdot}H_2O$	100	3.5	(*R*)

[a] The reactions were carried out on a 0.5 mmol scale, 12 mol % of the respective alkaloid, 10 mol % of $Cu(OAc)_2{\cdot}H_2O$, 10 equiv of CH_3NO_2 in *i*-PrOH (2 mL) at 0 °C for 3 days.
[b] Enantiomeric excess determined by HPLC analysis.
[c] Determined by comparison of the specific rotation sign and retention time (chiral HPLC) with the literature values.

Since the quinine/copper acetate system was catalytically effective, we decided to examine it more closely. When copper acetate dissolved in isopropyl alcohol was treated with an equimolar amount of quinine, a green complex precipitated slowly. The subsequent addition of nitromethane made a homogeneous solution, thus forming the other complexed species.

Little information on the coordination chemistry of copper(II) cations–quinine system has appeared in the literature.[6] Recently, three different coordination modes have been suggested and two of them correspond to a 1:1 copper to ligand ratio. However, more detailed structures remain obscure and our attempts to obtain a crystal suitable for the X-ray study were unsuccessful.

In order to gain additional information on the catalytic system, we carried out the model reaction with different amounts of quinine and quinine used with its pseudoenantiomer (quinidine) and diastereomer (*epi*-quinine) (Table 2).

The results shown in Table 2 suggest that the enantioselective reaction is catalyzed by a quinine–$Cu(OAc)_2$ 1:1 complex. An excess of the ligand lowers the ee, while the total yield increases. This is in agreement with the outcome observed in the presence of only quinine (Table 1, entry 8). When using $Cu(OAc)_2$ with a mixture of 70% quinine and 30% quinidine (its pseudoenantiomer) we obtained an ee value (entry 8) close to the expected value for two independent and parallel processes catalyzed by each complex [calculated 43%, (*S*)]. A mixture of quinine and *epi*-quinine (entry 7) gave a result close to the corresponding estimated one [61% (*S*)]. Thus, it seems that all the *Cinchona* alkaloid–$Cu(OAc)_2$ 1:1 complexes accommodate both reactants (aldehyde and nitronate anion), thus facilitating the reaction, although the enantioselectivity depends on the stereochemical match within the particular diastereomeric arrangement.

Table 2
Nitroaldol reaction of benzaldehyde and nitromethane catalyzed by quinine/$Cu(OAc)_2$[a]

Entry	Ligand added	Amount (mol %)	Yield (%)	ee [b](%) configuration[c]
1	(8*S*,9*R*)-Quinine	5	51	76 (*S*)
2	(8*S*,9*R*)-Quinine	8	56	77 (*S*)
3	(8*S*,9*R*)-Quinine	10	78	79 (*S*)
4	(8*S*,9*R*)-Quinine	12	87	86 (*S*)
5	(8*S*,9*R*)-Quinine	16	89	66 (*S*)
6	(8*S*,9*R*)-Quinine	24	91	57 (*S*)
7	(8*S*,9*R*)-Quinine	8.4		
	(8*S*,9*S*)-*epi*-Quinine	3.6	73	56 (*S*)
8	(8*S*,9*R*)-Quinine	8.4		
	(8*R*,9*S*)-Quinidine	3.6	68	49 (*S*)

[a] The reactions were carried out on a 0.5 mmol scale, in the presence of quinine, $Cu(OAc)_2{\cdot}H_2O$ (10 mol %) in *i*-PrOH (2 mL) at 0 °C for 3 days.
[b] Enantiomeric excess determined by HPLC analysis.
[c] Determined by comparison of the sign of specific rotation and retention time (chiral HPLC) with the literature values.

With the simple catalytic system in hand, we carried out a Henry reaction between nitromethane and several different aldehydes; in all but two cases we obtained the respective nitroalcohols in reasonable to good ee and yield (Table 3). For *trans*-cinnamaldehyde, the yield was less due to side-reactions while for *o*-nitrobenzaldehyde the enantioselectivity observed was poor.

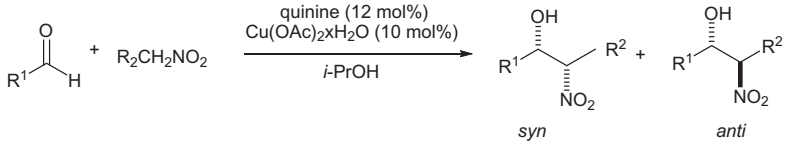
Table 3
Nitroaldol reaction of aldehydes and nitromethane catalyzed by quinine/$Cu(OAc)_2$[a]

Entry	RCHO	Yield (%)	ee [b](%) configuration[c]
1	Ph	87	86 (*S*)
2	*o*-$NO_2C_6H_4$	86	15 (*S*)
3	*o*-$MeOC_6H_4$	88	67 (*S*)
4	9-Anthryl	50	68 (*S*)
5	PhCH=CH	17	61 (*S*)
6	*c*-C_6H_{11}	63	72 (*S*)
7	*n*-C_5H_{11}	62	71 (*S*)
8	*iso*-C_4H_9	57	83 (*S*)
9	*tert*-C_4H_9	52	75 (*S*)

[a] The reactions were carried out on a 0.5 mmol scale, in the presence of quinine (12 mol %), $Cu(OAc)_2{\cdot}H_2O$ (10 mol %) in *i*-PrOH (2 mL) at 0 °C for 3 days.
[b] Enantiomeric excess determined by HPLC analysis.
[c] Determined by comparison of the specific rotation sign and retention time (chiral HPLC) with the literature values.

These results prompted us to extend this reaction to other nitroalkanes and to examine the diastereoselectivity (Scheme 2, Table 4).

The reaction of nitroethane with benzaldehyde was carried out as before in the presence of quinine/$Cu(OAc)_2$ at 0 °C to mainly give the *syn*-product in 78% ee. Lowering temperature to −20 °C led to an improvement in both diastereo- and enantioselectivities with no decrease in the yield (Table 4, entry 2). The addition of nitroethane to cyclohexanecarboxaldehyde at −20 °C gave the *syn*-nitroaldol in 60% yield with 82% de and 94% ee (entry 4). However, when 1-nitropropane was used in this reaction, lowering the temperature resulted in a large decrease in the yield with a less pronounced improvement of selectivity (entries 5 and 6). Finally, the reaction of 9-anthraldehyde with 1-nitropropane (entry 7) afforded both the *syn*- (main) and *anti*-product in 82% and 70% ee,



Scheme 2.

Table 4
Henry reaction of aldehydes and nitroalkanes catalyzed by quinine/$Cu(OAc)_2$[a]

Entry	R_1	R_2	T (°C)	Yield[b] (%)	dr[c] [*syn*/*anti*]	ee[d,e] [*syn*] (%)	ee[d,e] [*anti*] (%)
1	Ph	CH_3	0	99	65:35	78 (1*S*,2*S*)	46 (1*S*,2*R*)
2	Ph	CH_3	−20	98	76:24	94 (1*S*,2*S*)	71 (1*S*,2*R*)
3	*c*-C_6H_{11}	CH_3	0	99	83:17	88 (1*S*,2*S*)	62 (1*S*,2*R*)
4	*c*-C_6H_{11}	CH_3	−20	60	91:9	94 (1*S*,2*S*)	63 (1*S*,2*R*)
5	*c*-C_6H_{11}	CH_3CH_2	0	62	81:19	81 (1*S*,2*S*)	60 (1*S*,2*R*)
6	*c*-C_6H_{11}	CH_3CH_2	−20	39	86:14	88 (1*S*,2*S*)	66 (1*S*,2*R*)
7	9-Anthryl	CH_3CH_2	0	87	81:19	82 (1*S*,2*S*)	70 (1*S*,2*R*)

[a] The reactions were carried out on a 0.5 mmol scale, 12 mol % of quinine, 10 mol % of $Cu(OAc)_2 \cdot H_2O$, 10 equiv of nitroalkane in *i*-PrOH (2 mL) for 3 days.
[b] Combined yields of *syn* and *anti* isomers.
[c] Determined by ^1H NMR spectroscopy of the crude product.
[d] Determined by chiral HPLC.
[e] The absolute configurations were established by comparison with literature data.

respectively. When the reaction was carried out at −20 °C, it was completely halted. The last diastereomeric products were separated by chromatography to give pure *syn*- and *anti*-isomers in 90% and 97% ee, correspondingly.

3. Conclusion

In conclusion, we have found that a simple catalytic system made of quinine and copper acetate increases the diastereoselectivity and enantioselectivity of Henry reactions of aromatic and aliphatic aldehydes with nitromethane and its α-substituted derivatives.

4. Experimental

4.1. General

^1H NMR and ^{13}C NMR spectra were measured on a Bruker CPX (^1H, 300 MHz) spectrometer using TMS as the internal standard. The reported coupling constants were directly observed on the spectra. IR spectra were recorded on a Perkin–Elmer 1600 FTIR spectrophotometer. Optical rotations at 578 nm were measured using an Optical Activity Ltd Model AA-5 automatic polarimeter. The enantiomeric composition of the nitroaldols was determined by HPLC analysis using a chiral stationary phase (Chiracel OD-H or Daicel Chiralpak AD-H). The absolute configuration was assigned by comparison of the retention time and the sign of the specific rotation with the literature data. The absolute stereochemistry of both diastereomers was assigned by comparison of the retention times in HPLC to the literature data. Diastereomeric ratios of the *syn*/*anti* products were determined using ^1H NMR spectroscopy. High-resolution mass spectra (HRMS) were recorded on a Waters LCD Premier XE HRMS apparatus using ESI technique. Separations of products by chromatography were performed on Silica Gel 60 (230–400 mesh) purchased from Merck. *Cinchona* alkaloids were commercially available, *epi*-quinine and *epi*-quinidine were prepared according to a general procedure described in Ref. 7. Liquid aldehydes were freshly distilled before use.

4.2. General procedure for the nitroaldol reaction

The ligand (0.06 mmol, 12 mol %) and $Cu(OAc)_2 \cdot H_2O$ (10.0 mg, 0.05 mmol, 10 mol %) were dissolved in *i*-PrOH (1 mL) and the mixture was stirred for 3 h at rt to give a blue-green solution. The reaction mixture was cooled to 0 °C (or −20 °C). The respective aldehyde (0.5 mmol, 1 equiv) and nitroalkane (5.0 mmol, 10 equiv) were added with an additional 1 mL of *i*-PrOH. After 3 days, the crude product was isolated by column chromatography (hexane/AcOEt 6:1) to give β-nitroalcohol or desired β-nitroalcohols as a mixture of diastereomers.

4.2.1. 2-Nitro-1-phenylethan-1-ol

The enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane/*i*-PrOH 90:10, 1.0 mL/min, λ = 225 nm, enantiomer (*R*) R_t = 13.9 min, enantiomer (*S*) R_t = 17.3 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2d,g,i,k,8,9] The spectroscopic data were in accord with the literature values.[2d,i–k,8]

4.2.2. 1-(2-Nitrophenyl)-2-nitroethan-1-ol

The enantiomeric excess was determined by HPLC (Chiralpak OD-H), hexane/*i*-PrOH 90:10, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 14.9 min, major enantiomer (*S*) R_t = 16.8 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2i,8] The spectroscopic data were in accord with the literature values.[2i,j,8]

4.2.3. 1-(2-Methoxyphenyl)-2-nitroethan-1-ol

The enantiomeric excess was determined by HPLC (Chiralpak OD-H), hexane/*i*-PrOH 90:10, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 12.4 min, major enantiomer (*S*) R_t = 14.9 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2i,9] The spectroscopic data were in accord with the literature values.[2i,j,8]

4.2.4. 1-(Anthracene-9-yl)-2-nitroethan-1-ol

The enantiomeric excess was determined by HPLC (Chiralpak OD-H), hexane/*i*-PrOH 90:10, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 16.8 min, major enantiomer (*S*) R_t = 26.5 min; $[\alpha]_D$ = −10.5 (*c* 0.16, CH_2Cl_2, 68% ee). The absolute configuration was assigned by analogy to other compounds in this work. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.03 (d, *J* = 3.2 Hz, 1H, O*H*), 4.54 (dd, *J* = 13.5, 2.8 Hz, 1H, C*H*NO_2), 5.35 (dd, *J* = 13.5, 10.6 Hz, 1H, C*H*NO_2), 6.98 (dd, *J* = 10.6, 2.8 Hz, 1H, C*H*OH), 7.46–7.53 (m, 4H, ArH), 7.95–8.00 (m, 2H, ArH), 8.46 (s, 1H, ArH), 8.56 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.3, 79.6, 123.6, 124.5, 125.2, 125.5, 126.8, 126.9, 127.5, 129.3, 129.6, 130.5, 131.6, 133.5, 134.1, 135.7. IR (film): 3454, 3064, 2926, 1557, 1379, 1316, 1094, 734, 694 cm^{-1}. HRMS (ESI(−), $[M-H^+]^-$) calcd for $[C_{16}H_{13}NO_3-H^+]^-$ 266.0817; found 266.0835.

4.2.5. (*S*,*E*)-1-Nitro-4-phenylbut-3-en-2-ol

The enantiomeric excess was determined by HPLC (Chiralpak AD-H), hexane/*i*-PrOH 95:5, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 35.1 min, major enantiomer (*S*) R_t = 36.5 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2i,l,9] The spectroscopic data were in agreement with the literature values.[2d,i,j,l,9]

4.2.6. 1-Cyclohexyl-2-nitroethan-1-ol

The enantiomeric excess was determined by HPLC (Chiralpak AD-H), hexane/*i*-PrOH 97:3, 0.8 mL/min, λ = 225 nm, minor enantiomer (*R*) R_t = 27.7 min, major enantiomer (*S*) R_t = 29.5 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2k,8,9] The spectroscopic data were in agreement with the literature values.[2d,k,l,8]

4.2.7. 1-Nitroheptan-2-ol

The enantiomeric excess was determined by HPLC (Chiralpak AD-H), hexane/*i*-PrOH 98:2, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 30.9 min, major enantiomer (*S*) R_t = 41.6 min. The absolute configuration was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2a,l] The spectroscopic data were in agreement with the literature values.[2a,l]

4.2.8. 4-Methyl-1-Nitropentan-2-ol

The enantiomeric excess was determined by HPLC (Chiralpak AD-H), hexane/*i*-PrOH 95:5, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 11.8 min, major enantiomer (*S*) R_t = 16.6 min. The absolute stereochemistry was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2i,l] The spectroscopic data were in agreement with the literature values.[2i,l]

4.2.9. 3,3-Dimethyl-1-nitrobutan-2-ol

The enantiomeric excess was determined by HPLC (Chiralpak OD-H), hexane/*i*-PrOH 95:5, 1.0 mL/min, λ = 210 nm, minor enantiomer (*R*) R_t = 16.2 min, major enantiomer (*S*) R_t = 18.3 min. The absolute stereochemistry was assigned by comparison of the retention times in HPLC and specific rotation signs with the literature data.[2g,l,8] The spectroscopic data were in agreement with the literature values.[2d,l]

4.2.10. 2-Nitro-1-phenylpropan-1-ol

Chiralpak AD-H, *n*-hexane/*i*-PrOH 95:5, 1 mL/min, λ = 225 nm, $anti_{major}$ (1*S*,2*R*) R_t = 13.0, $anti_{minor}$ (1*R*,2*S*) R_t = 14.5, syn_{major} (1*S*,2*S*) R_t = 17.9, syn_{minor} (1*R*,2*R*) R_t = 19.9 min.

Diastereomeric ratios (*syn*/*anti*) were determined by ^{1}H NMR. The absolute configuration of both diastereomers was assigned by comparison of the retention times in HPLC with the literature data.[2d–f,j,l] ^{1}H NMR spectroscopic data were in agreement with the literature values.[2i,k]

4.2.11. 1-Cyclohexyl-2-nitropropan-1-ol

Chiralpak AD-H, *n*-hexane/*i*-PrOH 95:5, 0.8 mL/min, λ = 225 nm, $anti_{minor}$ (1*R*,2*S*) R_t = 14.0, $anti_{major}$ (1*S*,2*R*) R_t = 15.9, syn_{major} (1*S*,2*S*) R_t = 15.1, syn_{minor} (1*R*,2*R*) R_t = 20.9 min.

Diastereomeric ratios (*syn*/*anti*) were determined by ^{1}H NMR spectroscopy. The absolute configuration of both diastereomers was assigned by comparison of the retention times in HPLC with the literature data.[4b,10a,d,e] The chemical shifts of protons adjacent with carbons C-1, C-2 as well as methyl groups were in agreement with those reported in the literature.[4b,10a,d,e]

4.2.12. 1-Cyclohexyl-2-nitrobutan-1-ol

Chiralpak AD-H, *n*-hexane/*i*-PrOH 97:3, 0.5 mL/min, λ = 210 nm, $anti_{minor}$ (1*R*, 2*S*) R_t = 25.9, $anti_{major}$ (1*S*,2*R*) R_t = 26.5, syn_{major} (1*S*,2*S*) R_t = 28.9, syn_{minor} (1*R*,2*R*) R_t = 46.2 min.

Diastereomeric ratios (*syn*/*anti*) were determined by ^{1}H NMR. Absolute configuration of both diastereomers was assigned by comparison of the retention times in HPLC with the literature data.[4b,10b,e] The chemical shifts of protons adjacent to carbons C-1, C-2 as well as methyl groups were in agreement with those reported in the literature.[4b,10b,e]

4.2.13. 1-(Anthracene-9-yl)-2-nitrobutan-1-ol

Chiracel OD-H, *n*-hexane/*i*-PrOH 97:3, 0.8 mL/min, λ = 225 nm, $anti_{minor}$ (1*R*,2*S*) R_t = 16.3, $anti_{major}$ (1*S*,2*R*) R_t = 12.3, syn_{major} (1*S*,2*S*) R_t = 28.2, syn_{minor} (1*R*,2*R*) R_t = 30.8 min. The absolute configurations of both diastereomers were determined by analogy to published HPLC retention times of similar compounds.[4b,10c] The mixture of diastereomers was separated using chromatography giving diastereomerically pure nitroaldols:

4.2.13.1. *syn*-(1*S*,2*S*)-1-(Anthracene-9-yl)-2-nitrobutan-1-ol. Solidified brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.71 (t, *J* = 7.3 Hz, 3H, CH_3), 1.52–1.63 (m, 1H, CHCH*H*CH_3), 1.80–1.84 (m, 1H, CHC*H*HCH_3), 2.76 (br s, 1H, OH), 5.47 (dt, *J* = 10.2, 3.1 Hz, 1H, C*H*NO_2), 6.66 (dd, *J* = 10.1, 3.1 Hz, 1H, C*H*OH), 7.47–7.56 (m, 4H, ArH), 7.97 (t, *J* = 8.1 Hz, 2H, ArH), 8.38–8.49 (m, 2H, ArH), 8.50 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 24.4, 71.4, 94.7, 123.6, 125.0, 125.7, 127.2, 128.0, 129.2, 129.3, 129.6, 129.9, 130.1, 131.1, 132.2, 133.5, 134.1. IR (film): 3479, 3054, 2973, 2936, 1557, 1373, 1284, 735, 694 cm^{-1}. HRMS (ESI(−), $[M-H^+]^-$) calcd for $[C_{18}H_{17}NO_3-H^+]^-$ 294.1130; found 294.1105.

The reaction mixture was purified using column chromatography (silica gel, *n*-hexane/AcOEt, 7:1), and gave mainly the *syn*-isomer in the first fraction (*syn*/*anti* 96:4 dr, 90% ee, 86 mg, 58% yield, $[\alpha]_D$ = +5.5 (*c* 0.18, CH_2Cl_2). The *anti*-isomer was isolated in the third fraction (*syn*/*anti* 5:95 dr, 97% ee, 17 mg, 12% yield).

4.2.13.2. *anti*-(1*S*,2*R*)-1-(Anthracene-9-yl)-2-nitrobutan-1-ol. Solidified yellow oil, $[\alpha]_D$ = +16.2 (*c* 0.11, CH_2Cl_2, 97% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, *J* = 7.3 Hz, 3H, CH_3), 2.39–2.54 (m, 2H, C*H*$_2$$CH_3$), 2.78 (br s, 1H, OH), 5.36 (dt, *J* = 10.7, 3.3 Hz, 1H, C*H*NO_2), 6.60 (d, *J* = 7.4 Hz, 1H, C*H*OH), 7.46–7.59 (m, 4H, ArH), 8.02 (d, *J* = 8.4 Hz, 2H, ArH), 8.47 (s, 1H, ArH), 8.48–8.58 (m, 2H, ArH).

Acknowledgments

We are grateful to the Polish Ministry of Science and Higher Education for financial support, Grant No. N204 161036.

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