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Efficient Nitro-Aldol Reaction Using SmI_2: A New Route to Nitro Alcohols under Very Mild Conditions

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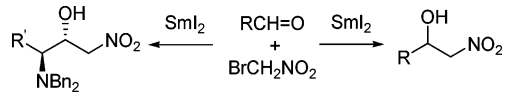

A novel method to obtain racemic 1-nitroalkan-2-ols by reaction of bromonitromethane with a variety of aldehydes and promoted by SmI_2 is reported. On the basis of these results, the chiral version has also been performed with chiral *N*,*N*-dibenzyl amino aldehydes, affording the corresponding enantiopure 3-amino-1-nitroalkan-2-ols with good stereoselectivity.

Introduction

Since its introduction into organic synthesis, the nitro-aldol reaction[1] has become one of the most useful methodologies for generating C−C bonds and obtaining polyfunctionalized molecules. The synthetic utility of the nitro-aldol reaction is based on the versatility of the 1,2-nitro alcohols that are obtained, which can be converted into 1,2-amino alcohols, amino sugars, nitroketones, nitroalkenes, ketones (Nef reaction), and other important compounds.[2] Particularly, nitroaldol adducts of enantiopure α-amino aldehydes can be readily converted into pharmacologically important molecules such as the anti-HIV drug amprenavir as well as α-hydroxy-*β*-amino acids, a valuable backbone of peptide mimetics.[3] However, to prepare nitroaldol adducts from enantiopure α-amino aldehydes, chiral catalysts or high pressures generally were necessary.[4] Only in one of these cases, enantiomeric excess of nitroaldol products, determined by chiral HPLC analysis, was reported.[4a]

In view of its significance, there are several reviews concerning the Henry reaction.[5] The nitroaldol reaction is generally performed in the presence of bases such as sodium methoxide, sodium hydroxide, sodium carbonate, barium hydroxide, tetrabutylamonium hydroxide, triethylamine, LDA, or butyllithium.[2,5] Consequently, when the starting carbonyl compound or the 1,2-nitro alcohol products are sensitive to the presence of bases, other byproducts can contaminate the target 1,2-nitro alcohols. For this reason, alternative procedures for the preparation of Henry-type adducts that obviate the use of bases would be of great interest.[6]

Introduced by Kagan in 1977,[7] samarium diiodide has been used to perform various organic reactions, chiefly carbon−carbon bond formation.[8] However, to the best of our knowledge, the synthesis of nitro alcohols (Henry adducts) by using samarium diiodide has not been yet described.

In this paper, we describe a novel synthesis of racemic 1-nitroalkan-2-ols **3** by reaction of bromonitromethane[9] with various aldehydes promoted by SmI_2, respectively. This process take place under very mild reaction conditions. On the basis of these results, the chiral version of this transformation has also been performed on chiral *N*,*N*-dibenzylamino aldehydes derived from alanine, phenylalanine, and leucine, affording the corresponding 3-amino-1-nitroalkan-2-ols in high yield and good stereoselectivity.

Results and Discussion

The initial studies on the preparation of racemic nitroalkan-2-ols were performed using 2.5 equiv of SmI_2.[10] Thus, the treatment of a solution of bromonitromethane (1.0 equiv) and

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SCHEME 1. Synthesis of Nitro Alcohols 3

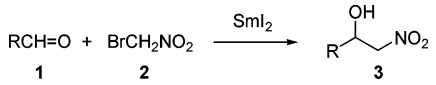


TABLE 1. Synthesis of Nitro Alcohols 3

entry	3	R	yield (%)[a]
1	**3a**	*n*-C_7H_{15}	>99
2	**3b**	Cy	90
3	**3c**	*i*-Bu	95
4	**3d**	*s*-Bu	93
5	**3e**	*t*-Bu	91
6	**3f**	C_9H_{17}[b]	50
7	**3g**	$PhCH_2$[c]	92
8	**3h**	Ph[c,d]	55
9	**3i**	-$(CH_2)_5$-	69
10	**3j**	*o*-$NO_2C_6H_4$[c,e]	54
11	**3k**	*m*-ClC_6H_4[c,e]	51

[a] Yield of the corresponding isolated pure products **3** based on compounds **1**. [b] $Me_2C{=}CH(CH_2)_2CH(Me)CH_2$. [c] The reaction was performed using SmI_3 instead of SmI_2. In this case, a longer reaction time (18 h) was required. [d] Compound purified by distillation. [e] Compounds purified by flash column chromatography.

various aldehydes (1.0 equiv) in THF, with SmI_2, at room temperature afforded the corresponding nitro alcohol **3** in high yield (Scheme 1).

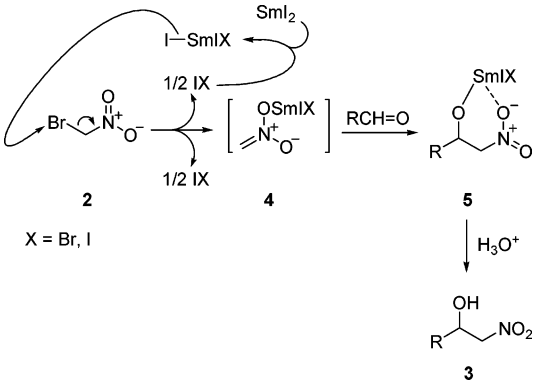
Surprisingly, comparable yields of compounds **3** were obtained when the reaction was carried out with sub-stoichiometric amounts (1.0, 0.5, or 0.35 equiv) of samarium diiodide under the same reaction conditions. When this reaction was carried out using lower amounts of SmI_2 (0.1 equiv), a mixture of **3**, aldehyde, and bromonitromethane was obtained. This latest result served to discard a samarium-promoted catalytic process.

Generally, cleaner reaction crudes were obtained when 1.0 equiv of SmI_2 was employed rather than 0.5 or 0.35 equiv. Consequently, the reactions were carried out with 1.0 equiv of SmI_2, and the results are shown in Table 1. The crude reaction products were obtained with high purity after solvent removal under vacuum and filtration through a pad of Celite (Table 1, entries 1−7 and 9). Only column chromatography purification was necessary when the reaction was performed with 0.5 or 0.35 equiv of SmI_2.

The reaction is general as shown by the results compiled in Table 1. Linear, branched, cyclic, and aromatic aldehydes were successfully used as starting materials. This process can also be carried out using readily enolizable aldehydes (Table 1, entry 7), and some other functionalities were compatible with this transformation, such as the nitro group, chlorine atom, and C−C double bonds (Table 1, entries 6, 10, and 11). When electron-rich substituted aryl aldehydes such as *p*-anisaldehyde (*p*-MeO−$C_6H_4CH{=}O$) or *p*-$NMe_2-C_6H_4CH{=}O$ were utilized, no reaction took place. Finally, it is noteworthy that, in contrast to other previously described methods, the reaction can be performed with both hindered aldehydes and cyclic ketones such as pivaldehyde **1e** and cyclohexanone **1i** (Table 1, entries 5 and 9, respectively).

The synthesis of nitro alcohols **3** using an amount <2.0 equiv of SmI_2 is inconsistent with the typical SmI_2 role as monoelectronic reducing agent in Barbier-type processes. Alternatively, the reaction might be promoted by the iodide released by the

SCHEME 2. Mechanistic Proposal



SmI_3 traces, which are present in the THF solutions of samarium diiodide, as suggested by other works previously published.[11] To prove the latest hypothesis, the reaction of octanal **1a** and bromonitromethane **2** was carried out with SmI_3 (1.0 equiv) instead of SmI_2, the corresponding 1-nitrononan-2-ol **3a** being isolated in 89% yield.[12] Moreover, nitro alcohols that could not be obtained with SmI_2 (phenylacetaldehyde, benzaldehyde, *o*-nitrobenzaldehyde, and *m*-chlorobenzaldehyde) were prepared using SmI_3. So, the use of SmI_3 could be a valuable alternative to the use of SmI_2.

Taking into account that reactions performed with SmI_2 afforded cleaner crudes than those when SmI_3 was used, all reactions were carried out using SmI_2. When compounds **3** were not obtained using SmI_2, they were performed with SmI_3 (see Table 1, entries 7, 8, 10, and 11).

Based on these observations we disclose the following mechanism to explain the synthesis of nitro alcohols **3**. The reaction could be triggered by traces of the SmI_3 present in the solution of SmI_2 in THF. So, SmI_3 could release iodide, which might attack the bromine atom of the bromonitromethane, generating IBr and promoting the addition of the nitronate anion **4** to the corresponding carbonyl compound (Scheme 2). The IBr generated could transform the SmI_2 into SmI_3 or SmI_2Br, which would continue the reaction. Moreover, the generated samarium alcoholate "$ROSmI_2$" or "ROSmIBr" **5**, could also act (similarly to SmI_3 or SmI_2Br) as source of iodide, and after two successive iodide-releases would generate species such as "$(RO)_3Sm$" that would afford compounds **3** after hydrolysis. This proposed mechanism is in agreement with the use of sub-stoichiometric amounts of SmI_2 or SmI_3 (0.5 or 0.35 equiv).

The obtained results in the synthesis of racemic nitro alcohols **3** prompted us to test the possible application of this method for synthesizing enantiopure 3-amino-1-nitroalkan-2-ols. When this transformation was performed on chiral *N*,*N*-dibenzylamino aldehydes **6**, under the same reaction conditions, the corresponding 3-amino-1-nitroalkan-2-ols **7** were obtained in high yields and with a good diastereoisomeric ratio (dr) (Scheme 3, Table 2).

The stereoselectivity of the reaction was determined by ^1H NMR spectroscopy (300 MHz) on the crude products **7**. The mixture of diastereoisomers obtained was easily separated. After

(10) The solution of SmI_2 in THF was rapidly obtained by reaction of diiodomethane with samarium powder in the presence of sonic waves: Concellón, J. M.; Rodríguez-Solla, H.; Bardales, E.; Huerta, M. *Eur. J. Org. Chem.* **2003**, 1775−1778.

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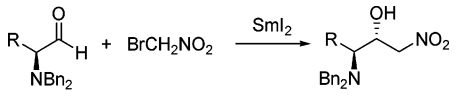
(12) When this process was performed with 1.0, 0.5, and 0.35 equiv of SmI_3, **3a** was similarly obtained with a yield ranging between 72% and 89%.

SCHEME 3. Synthesis of (2*R*,3*S*)-3-Amino-1-nitroalkan-2-ols 7



6 **2** **7**

TABLE 2. Synthesis of Products 7

			dr (%)[b]		yield (%)[c]	
entry	**7**[a]	R	crude	purified[d]	crude	purified[d]
1	**7a**	Me	85	>95	quant	70
2	**7b**	Bn	77	>95	quant	68
3	**7c**	*i*-Bu	62	>95	quant	61

[a] Enantiomeric excess (ee) >98% was determined by chiral HPLC (Chiracel OD-H) analysis. [b] Diastereoisomeric ratio (dr) determined by 300 MHz ^{1}H NMR analysis. [c] Yield of the corresponding isolated pure products based on compounds **6**. [d] Purified by flash column chromatography.

conventional column chromatography, pure compounds **7** were obtained with a diastereoisomeric ratio >95%.

The absolute configuration of **7** was established by comparison of the spectroscopic data of **7b** with those previously reported in the literature for the same compound.[3d] Structures of **7a** and **7c** (Table 2) were assigned by analogy.[13]

The enantiomeric purity of compounds **7** was determined by chiral HPLC chromatography of **7a**, showing an enantiomeric excess (ee) >98%. A racemic mixture of **7a** was prepared from racemic alaninal **6a** to exclude the possibility of coelution of both enantiomers in HPLC.[14]

Conclusions

In conclusion, we have described a novel reaction of bromonitromethane with a variety of aldehydes in very mild conditions promoted by SmI_2 to afford nitroalkan-2-ols. Starting from chiral *N*,*N*-dibenzyl aminoaldehydes, the corresponding enantiopure (2*R*,3*S*)-3-amino-1-nitroalkan-2-ols were obtained with good stereoselectivity. Other synthetic applications of these reactions, studies directed toward fully delineating the factors involved in these transformations, and attempts to develop the catalytic version of this process are currently under investigation within our laboratory.

Experimental Section

General Procedure. SmI_2 or SmI_3 (0.8 mmol, 1 equiv) in THF (8 mL) was added to a stirred solution of bromonitromethane **2** (0.8 mmol, 1 equiv) and the corresponding carbonyl compound **1** or **6** (0.8 mmol, 1 equiv) in THF (5 mL). After stirring the reaction at room temperature for 2 h it was quenched with aqueous HCl (10 mL, 0.1 M) before the organic material was extracted with dichloromethane. The combined extracts were washed with an aqueous saturated solution of $Na_2S_2O_3$ and then dried over Na_2SO_4, and the solvent was removed under reduced pressure, affording compounds **3** or **7**.

1-Nitrononan-2-ol (3a). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.40 (dd, J = 3.4, 12.5 Hz, 1H), 4.37−4.30 (m, 1 H), 4.29−4.24 (m, 1 H), 3.29 (br s, 1 H), 1.56−1.19 (m, 12 H), 0.82 (t, J = 6.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 80.5 (CH_2), 68.6 (CH), 33.6 (CH_2), 31.55 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.0 (CH_2), 22.4 (CH_2), 13.8 (CH_3). HRMS: calcd for [$C_9H_{19}NO_3$ − OH] 172.1338, found 172.1335. IR (neat): 3409, 2902, 1555, 1466, 1380 cm^{-1}. R_f 0.3 (hexane/EtOAc 5/1).

1-Cyclohexyl-2-nitroethanol (3b). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.47 (dd, J = 3.4, 13.1 Hz, 1H), 4.40 (dd, J = 8.5, 13.1 Hz, 1H), 4.10−4.04 (m, 1H), 2.5 (s, 1H), 1.83−0.99 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 79.2 (CH_2), 72.7 (CH), 41.3 (CH), 28.6 (CH_2), 27.8 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 25.6 (CH_2). MS (70 eV) *m*/*z* (%): 127 (<1) [M − NO_2]$^+$, 83 (75), 55 (100), 41 (52). IR (neat): 3422, 2927, 1555, 1450, 1385 cm^{-1}. R_f 0.3 (hexane/EtOAc 5/1). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.50; H, 8.67; N, 8.15

4-Methyl-1-nitropentan-2-ol (3c). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.40−4.31 (m, 3H), 2.94 (s, 1H), 1.88−1.72 (m, 1H) 1.51−1.39 (m, 2H), 0.93 (d, J = 6.3 Hz, 3H), 0.91 (d, J = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 80.9 (CH_2), 66.8 (CH), 42.3 (CH_2), 24.1 (CH), 22.9 (CH_3), 21.5 (CH_3). HRMS calcd for [$C_6H_{13}NO_3$ − OH] 130.0868, found 130.0865. IR (neat): 3417, 2960, 1557, 1469, 1386 cm^{-1}. R_f 0.3 (hexane/EtOAc 10/1).

3-Methyl-1-nitropentan-2-ol (3d). Mixture of diastereoisomers. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.50−4.18 (m, 4H), 2.71−2.45 (m, 2H), 2.10−2.33 (m, 2H), 1.45−1.62 (m, 4H), 1.12−1.35 (m, 6H), 0.76−0.99 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 79.5 (CH_2), 78.9 (CH_2), 72.3 (CH), 71.5 (CH), 38.3 (CH), 38.1 (CH), 25.4 (CH_2), 24.6 (CH_2), 14.4 (CH_3), 13.5 (CH_3), 11.4 (CH_3), 11.1 (CH_3). IR (neat): 3412, 2928, 1557, 1463, 1383 cm^{-1}. R_f 0.3 (hexane/EtOAc 5/1). Anal. Calcd for $C_6H_{13}NO_3$: C, 48.97; H, 8.90; N, 9.52. Found: C, 48.83; H, 9.01; N, 9.50.

3,3-Dimethyl-1-nitrobutan-2-ol (3e). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.51 (dd, J = 2.3, 13.1 Hz, 1H), 4.35 (dd, J = 10.2, 13.1 Hz, 1H), 4.01 (dd, J = 2.3, 10.2 Hz, 1H), 2.64 (s, 1H), 0.95 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 78.1(CH_2), 76.1 (CH), 34.1 (C), 25.4 (3 × CH_3). MS (70 eV) *m*/*z* (%): 131 (<1) [M − H_2O]$^+$, 87 (10), 57 (100), 41 (50), 29 (25). IR (neat): 3448, 2963, 1557, 1480, 1383 cm^{-1}. R_f 0.3 (hexane/EtOAc 5/1). Anal. Calcd for $C_6H_{13}NO_3$: C, 48.97; H, 8.90; N, 9.52. Found: C, 48.79; H, 9.20; N, 9.35.

4,8-Dimethyl-1-nitronon-7-en-2-ol (3f). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.06−5.01 (m, 2H), 4.42−4.23 (m, 4H), 4.13−3.92 (m, 2H), 2.04−1.82 (m, 4H), 1.63 (s, 6H), 1.55 (s, 6H), 1.43−1.04 (m, 10H), 0.91 (t, J = 6.3 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 131.3 (C), 131.2 (C), 124.1 (2 × CH), 81.7 (CH_2), 80.7 (CH_2), 66.8 (CH), 66.4 (CH), 40.8 (CH_2), 40.5 (CH_2), 37.3 (CH_2), 36.1 (CH_2), 28.7 (CH), 28.2 (CH), 25.3 (2 × CH_3), 25.1 (CH_2), 24.9 (CH_2), 19.7 (CH_3), 18.6 (CH_3), 17.4 (2 × CH_3). IR (neat): 3420, 2926, 1555, 1456, 1381 cm^{-1}. R_f 0.3 (hexane/EtOAc 5/1). Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.50; H, 9.71; N, 6.62

1-Nitro-3-phenylpropan-2-ol (3g). ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) have been compared with the data previously described in ref 15. IR (neat): 3422, 3014, 2975, 2921, 1561, 1425, 1382 cm^{-1}. R_f 0.4 (hexane/EtOAc 5/1).

1-Nitro-2-phenylethan-2-ol (3h). ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) have been compared with the data previously described in ref 15. IR (neat): 3430, 3050, 2981, 2926, 1555, 1420, 1375 cm^{-1}. R_f 0.4 (hexane/EtOAc 5/1).

1-(Nitromethyl)cyclohexanol (3i). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.47 (s, 2H), 2.93 (br s, 1H), 2.1−1.1 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 80.6 (CH_2), 70.7 (C), 34.8 (2 × CH_2), 25.1 (CH_2), 21.4 (2 × CH_2). HRMS calcd for [$C_7H_{13}NO_3$ − NO_2] 113.0966, found 113.0971. IR (neat): 3398, 2927, 1549, 1450, 1380 cm^{-1}. R_f 0.2 (hexane/EtOAc 5/1).

(13) The addition of the anion to **5** takes place under nonchelation control, in agreement with other previously reported addition of nucleophiles to *N*,*N*-dibenzyl α-aminoaldehydes: (a) Reetz, M. T. *Angew. Chem., Int. Ed.* **1991**, *30*, 1531−1546. (b) Reetz, M. T. *Chem. Rev.* **1999**, *99*, 1121−1162.

(14) Chiral HPLC analysis for **7a** shows ee > 98%: Chiracel-OD, UV detector 210 nm, 0.5 mL/min, 95/5 hexane/*i*-PrOH, t_R 37.5 min; racemic mixture t_R 34.9 and 37.5 min.

(15) Sorgedrager, M. J.; Malpique, R.; van Rantwijk, F.; Sheldon, R. A. *Tetrahedron*: *Asymmetry* **2004**, *15*, 1295−1299.

1-Nitro-2-(*o*-nitrophenyl)ethan-2-ol (3j). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10−7.49 (m, 4H), 6.02 (dd, J = 2.3, 9.0 Hz, 1H), 4.85 (dd, J = 2.3, 13.3 Hz, 1H), 4.55 (dd, J = 9.0, 13.3 Hz, 1H), 3.60 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.0 (C), 134.3 (CH), 134.1 (C), 129.5 (CH), 128.6 (CH), 124.8 (CH), 80.0 (CH_2), 66.7 (CH). MS (70 eV) *m*/*z* (%): 166 (<1) $[M - NO_2]^+$, 148 (55), 121 (50), 91 (64), 77 (95), 65 (100), 51 (63). IR (neat): 3585, 3015, 2986, 2927, 1558, 1529, 1418, 1377, 1348 cm^{-1}. R_f 0.25 (hexane/EtOAc 3/1). Anal. Calcd for $C_8H_8N_2O_5$: C, 45.29; H, 3.80; N, 13.20. Found: C, 45.15; H, 3.97; N, 13.18.

1-Nitro-2-(*m*-chlorophenyl)ethan-2-ol (3k). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44−7.27 (m, 4H), 5.46 (dd, J = 3.1, 7.8 Hz, 1H), 4.66−4.45 (m, 2H), 3.14 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.0 (C), 134.9 (C), 130.2 (CH), 129.0 (CH), 126.1 (CH), 124.0 (CH), 80.8 (CH_2), 70.2 (CH). MS (70 eV) *m*/*z* (%): 201 (10) $[M]^+$, 154 (100), 139 (60), 91 (68), 77 (86). IR (neat): 3424, 3056, 2987, 2926, 1557, 1421, 1378 cm^{-1}. R_f 0.2 (hexane/EtOAc 3/1). Anal. Calcd for $C_8H_8ClNO_3$: C, 47.66; H, 4.00; N, 6.95. Found: C, 47.81; H, 4.23; N, 7.06.

(2*R*,3*S*)-3-Dibenzylamine-1-nitrobutan-2-ol (7a). $[\alpha]^{25}_D$ = +18.1 (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41−7.27 (m, 10H), 4.87 (dd, J = 1.8, 13.5 Hz, 1H), 4.17−4.11 (m, 1H), 3.95−3.87 (m, 1H), 3.65 (syst. AB, d, J = 13.4 Hz, 2H), 3.28 (syst. AB, d, J = 13.4 Hz, 2H), 2.65−2.55 (m, 2H), 1.11 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.8 (2 × C), 128.8 (4 × CH), 128.5 (4 × CH), 127.3 (2 × CH), 79.7 (CH_2), 70.9 (CH), 55.2 (CH), 54.3 (2 × CH_2), 8.2 (CH_3). HRMS calcd for $[C_{18}H_{22}N_2O_3 - CH(OH)CH_2NO_2]$ 224.1439, found 224.1438. IR (neat): 3563, 3493, 3091, 2930, 1550, 1490, 1375 cm^{-1}. R_f 0.4 (hexane/EtOAc 3/1).

(2*R*,3*S*)-3-Dibenzylamine-1-nitro-4-phenylbutan-2-ol (7b). $[\alpha]^{25}_D$, ^{1}H NMR, ^{13}C NMR, and IR spectroscopical data were in accordance with those previously reported in ref 3d.

(2*R*,3*S*)-3-Dibenzylamine-5-methyl-1-nitrohexa-2-ol (7c). $[\alpha]^{25}_D$ = −2.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43−7.25 (m, 10H), 4.74 (dd, J = 1.4, 13.1 Hz, 1H), 4.47−4.41 (m, 1H), 4.16 (dd, J = 9.6, 13.1 Hz, 1H), 3.71 (syst. AB, d, J = 13.6 Hz, 2H), 3.61 (syst. AB, d, J = 13.6 Hz, 2H), 2.90 (br s, 1H), 2.78−2.69 (m, 1H), 1.97−1.84 (m, 1H), 1.77−1.66 (m, 1H), 1.45−1.31 (m, 1H), 0.99 (d, J = 6.5 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0 (2 × C), 128.8 (4 × CH), 128.4 (4 × CH), 127.2 (2 × CH), 79.9 (CH_2), 70.0 (CH), 56.9 (CH), 54.5 (2 × CH_2), 35.6 (CH_2), 25.5 (CH), 22.9 (CH_3), 22.7 (CH_3). IR (neat): 3465, 3058, 2951, 2923, 2867, 1609, 1552, 1495, 1378 cm^{-1}. R_f 0.45 (hexane/EtOAc 3/1). Anal. Calcd for $C_{21}H_{28}N_2O_3$: C, 70.76; H, 7.92; N, 7.86. Found: C, 71.01; H, 8.10; N, 7.99.

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Supporting Information Available: General procedures and copies of ^{13}C NMR spectra for compounds **3** and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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