First $TiCl_4$-Mediated Diastereoselective Reduction of α-Nitro Ketones to *Anti-β*-Nitro Alcohols by BH_3·SMe_2

Roberto Ballini,* Giovanna Bosica, Enrico Marcantoni, and Patrizia Vita

Dipartimento di Scienze Chimiche dell'Università, Via S. Agostino 1, I-62032 Camerino (MC), Italy

Giuseppe Bartoli*

Dipartimento di Chimica "A. Mangini" dell'Università, V.le Risorgimento 4, I-40136 Bologna, Italy

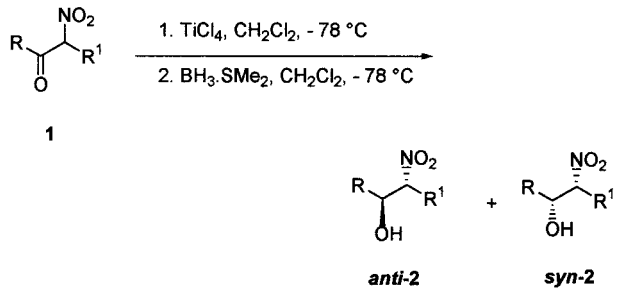
ballini@camserv.unicam.it

Received April 11, 2000

Introduction

β-Nitro alcohols are an important class of compounds frequently used as key intermediates in the construction of numerous natural products and other useful biologically active compounds.[1] Moreover, they are versatile building blocks in that the nitro group that can be readily reduced with retention of configuration[2] and the resulting amino alcohols are useful intermediates in the elaboration of pharmacologically important products and are also widely used in the preparation of chiral auxiliaries.[3] For these reasons the stereoselective synthesis of *β*-nitro alcohols continues to be an active area of research. The nitroaldol (Henry) reaction is one of the classical method by which diastereomeric mixtures of *β*-nitro alcohols are formed upon treatment of primary or secondary nitro alkanes and carbonyl derivatives with a base.[4] Although the Henry reaction has a remarkable ability to yield *β*-nitro alcohols, the levels of the stereoselectivity are usually low, and, to obtain better diastereoselectivity, it is necessary to carefully control the basicity of the reaction medium[5] or to use complexes as catalysts.[6] Furthermore, in these reactions *syn-β*-nitro alcohols are often formed predominantly over *anti*-diastereomers.[6,7] Thus, in continuation of our interest in the application of nitro aliphatics in synthesis, we decided to investigate the possible formation of *β*-nitro alcohols by stereoselective reduction of the corresponding α-nitro ketones, readily available from different sources,[8c,e] such as nitro alcohols,[8b,f] alkenes,[8g] carboxylic acid derivatives,[8a,d] and ketones.[8h,i]

Scheme 1



Results and Discussion

Studies performed in our laboratories have revealed that the reduction of α-nitro ketones **1** (Scheme 1) at low temperature (−78 °C) with borane−dimethyl sulfide (BH_3·SMe_2) in the presence of $TiCl_4$ is good to excellent *anti* selective (Table 1), and the sense of the stereocontrol may be predicted by invoking the cyclic Cram chelate model[9] for hydride delivery to the carbonyl moiety. This is clearly due to chelation by the titanium atom,[10] which creates a bridge between the oxygen atoms of the C=O and NO_2 groups. In the resulting six-membered cyclic intermediate, the most populated conformation **A** is preferentially attacked by the incoming hydride ion at the less-hindered side opposite R^1 (Scheme 2). It is obvious that every increase in bulkiness of R^1, shifting the conformational equilibrium toward the **A** conformation, increases the *anti*/*syn* ratio. It is reasonable that the addition should be performed at low temperature, i.e., under conditions where retro-nitroaldol reaction and epimerization at the $CHNO_2$ center are not effective.[11] A noncoordinating solvent like dichloromethane is crucial for maximizing the effect of $TiCl_4$; in fact, as previously reported,[12] a donor solvent like THF solvates this compound and nullifies its effect.

(1) (a) Hakomori, S. In *Handbook of Lipid Research Sphingolipid Biochemistry*; Kaufer, J. N., Hakomori, S., Eds.; Plenum Pres: New York, 1983; Vol. 1. (b) Williams, T. M.; Crumbie, R.; Mosher, H. S. *J. Org. Chem.* **1985**, *50*, 91−97. (c) Rosini, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, pp 321−339. (d) Ballini, R. In *Studies in Natural Products Chemistry*, Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, 1997; Vol. 19, pp 117−184. (e) Morgan, B.; Sarikonda, B. R.; Dodds, D. R.; Homan, M. J.; Vail R. *Tetrahedron: Asymmetry* **1999**, *10*, 3681−3690.

(2) (a) Barrett, A. G. M.; Spilling, C. D. *Tetrahedron Lett.* **1988**, *29*, 5733−5734. (b) Bordwell, F. G.; Garbisch, E. W. *J. Org. Chem.* **1963**, *28*, 1765−1769. (c) Bordwell, F. G.; Arnold, R. L. *J. Org. Chem.* **1962**, *27*, 4426−4428. (d) Nielsen, A. T. *J. Org. Chem.* **1962**, *27*, 1998−2001.

(3) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835−875.

(4) (a) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1−18. (b) Ballini, R.; Bosica, G. *J. Org. Chem.* **1997**, *62*, 425−427, and references therein.

(5) Bulbule, V. J.; Deshpande, V. H.; Velu, S.; Sudalai, A.; Sivasankar, S.; Sathe, V. T. *Tetrahedron* **1999**, *55*, 9325−9332.

(6) Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388−7389.

(7) (a) Eyer, M.; Seebach, D. *J. Am. Chem. Soc.* **1985**, *107*, 3601−3606. (b) Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418−4420. (c) Barrett, A. G. M.; Robyr, C.; Spilling, C. D. *J. Org. Chem.* **1989**, *54*, 1233−1234. (d) Kiyooka, S.; Tsutsui, T.; Maeda, H.; Kaneko, Y.; Isobe, K. *Tetrahedron Lett.* **1995**, *36*, 6531−6534.

(8) (a) Seebach, D.; Leher, F. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 505−506. (b) Rosini, G.; Ballini, R.; Sorrenti, P.; Petrini, M. *Synthesis* **1984**, 607−608. (c) Rosini, G.; Ballini, R. *Synthesis* **1988**, 833−847. (d) Ono, N.; Fujii, M.; Kaji, A. *Synthesis* **1987**, 532−535. (e) Rosini, G.; Ballini, R.; Petrini, M.; Marotta, E.; Righi, P. *Org. Prep. Proc. Int.* **1990**, *22*, 707−746. (f) Ballini, R.; Bosica, G.; Parrini, M. *Tetrahedron Lett.* **1998**, *39*, 7963−7964. (g) Venkat Ram Reddy, M.; Kumareswaran, R.; Vankar, Y. D. *Tetrahedron Lett.* **1995**, *36*, 7149−7152. (h) Rathore, R.; Lin, Z.; Kochi, J. K. *Tetrahedron Lett.* **1993**, *34*, 1859−1862. (i) Cushman, M.; Mathew, J. *Synthesis* **1982**, 397−399.

(9) (a) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748−2755. (b) Frye, S. V.; Eliel, E. L.; Cloux, R. *J. Am. Chem. Soc.* **1987**, *109*, 1862−1863. (c) Nichols, M. A.; McPhail, A. T.; Arnett, E. M. *J. Am. Chem. Soc.* **1991**, *113*, 6222−6233. (d) Still, W. C.; McDonald, J. H. *Tetrahedron Lett.* **1980**, *21*, 1031−1034. (e) Keck, G. E.; Abbott, D. E. *Tetrahedron Lett.* **1984**, *25*, 1883−1886. (f) Reetz, M. T., *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556−569.

(10) Reetz, M. T. In *Organometallics in Synthesis*; Schlosser, M., Ed.; John Wiley & Sons: Chichester, 1994; pp 195−282.

(11) Menzel, A.; Ohrlein, R.; Griesser, H.; Wehner, V.; Jäger, V. *Synthesis* **1999**, 1691−1702.

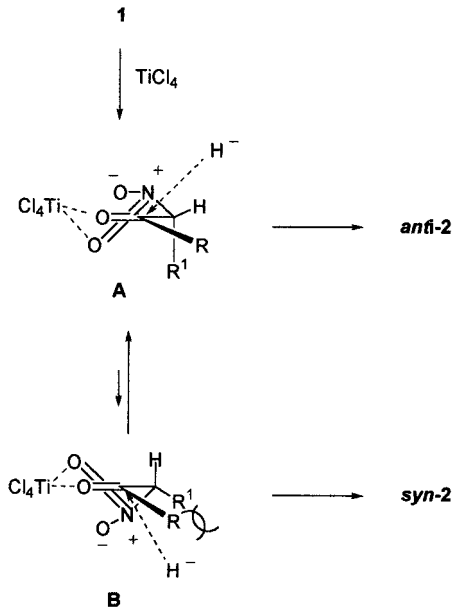
10.1021/jo000542z CCC: $19.00
Published on Web 08/10/2000

Table 1. Stereoselective Reduction of α-Nitro Ketones (1) to β-Nitro Alcohols (2)

entry	R	R^1	nitro ketone	overall yield (%)[c]	prod.[a]	*anti*/*syn*[b]
1	Ph	$CH_3(CH_2)_4$	**1a**[d]	95	**2a**	>99/1
2	$CH_3(CH_2)_3$	$(CH_3)_2CH$	**1b**[e]	96	**2b**	91/9
3	*p*-$NO_2C_6H_4$	CH_3	**1c**[f]	81	**2c**	90/10
4	$PhCH_2CH_2$	CH_3	**1d**[f]	> 99	**2d**	83/17
5	$CH_3(CH_2)_7$	$(CH_3)_2CHCH_2$	**1e**[e]	90	**2e**	75/25
6	$CH_3(CH_2)_{10}$	$CH_3(CH_2)_4$	**1f**[e]	98	**2f**	75/25
7	CH_3CH_2	$PhCH_2$	**1g**[d]	95	**2g**	76/24
8	$(CH_3)_2CH$	$CH_3CH_2CH_2$	**1h**[e]	89	**2h**	56/44
9	C_6H_{11}	$CH_3(CH_2)_3$	**1i**[d]	> 99	**2i**	54/46
10	Ph	CH_3	**1j**[g]	93	**2j**	91/9

[a] By adding the BH_3·SMe_2 complex to the CH_2Cl_2 solution of **1**/$TiCl_4$ complex at −78 °C. [b] Determined by ^1H and ^{13}C NMR spectroscopy. [c] Calculated on the mixture of diastereomers isolated by column chromatography. [d] Synthesized following the procedure in ref 8b. [e] Synthesized following the procedure in ref 8f. [f] Synthesized following the procedure in ref 8d. [g] Synthesized following the procedure in ref 8g.

Scheme 2



Although several types of amine boranes[13] are available for the reduction of α-alkyl-β-oxocarbonyl compounds, better results have been obtained when this reduction of α-nitro ketones was performed with borane−dimethyl sulfide reagent. In fact the reduction of compound **1a**, under our experimental conditions but with borane−pyridine as reducing agent, gives a high yield (98%), but a lower diastereoselectivity (*anti*/*syn* = 78/22). This is in consequence, in our opinion, of easy epimerization at the nitro-substituted C-atom due to the higher basicity of the amine borane reagent in comparison to BH_3·SMe_2.

In the literature the assignment for *anti* and *syn* diastereomers is based on the coupling constant between the α- and β-protons, which is usually larger for the *syn* than for the *anti* isomer.[14] To avoid confusion about the diastereomeric purity determined by NMR analysis, we have confirmed the assignment of configuration to our products by chemical correlation. Stereospecific reduction[2a] of compound **2j** gave the corresponding amino alcohol whose spectral data were all identical with that of an authentic sample of racemic norephedrine. In analogy, we assume that the other products (**2a**−**i**) also belong to the *anti* series. These assignments are in contrast to the assignments of the structures for compounds **2** made by cross-relaxation rates measured with two-dimensional NOE spectroscopy.[15] It was assumed that a hydrogen bond between the nitro group and the OH locks the structure in a semirigid conformation.[16] Indeed, no concentration effects were observed either in the IR absorptions or in the proton chemical shift values for the OH signals. Compound **2a** was submitted to a ROESY analysis,[17] but no interesting cross-peaks were detected at room temperature. At −50 °C, besides the expected ROE effects between the α-H−C and the β-H−C, interesting cross-peaks appeared between the α-H-C and one of the methylene hydrogen in the γ-position and between β-H-C and the aromatic ring protons. Certainly, these cross-peaks would be expected for a *syn* configuration. Since these six-membered cyclic conformations are more flexible than the corresponding cyclohexane derivatives,[18] we believe that a rapid ring inversion would generate an additional element of symmetry.[19] This process would render equivalent the axial and the equatorial hydrogen atoms, and thus the NOE cross-peaks in the 2D rotating-frame experiments are not indicative for the configuration of β-nitro alcohols. To support and clarify this interpretation of the results of ROESY analysis, compound *anti*-**2j**, of known configuration, was also submitted to a ROESY analysis at −50 °C, and the same kind of cross-peaks (between the α-H-C and the β-H-C, the α-H-C and CH_3, and the β-H-C and the aromatic ring protons), as for compound **2a**, were detected.

Finally, it should be noted that when R in α-nitro ketones **1** is an α-branched alkyl group such as cyclohexyl or isopropyl, the reduction shows a low diastereoselectivity (Table 1, entries 8 and 9). This demonstrates that the destabilizing gauche pentane interactions[20] reduce the unfavorable steric interactions between the two substituents in conformation **D** (Scheme 3).

In conclusion we have found efficient conditions for the reduction of α-nitro ketones to give the corresponding nitro alcohols. In some cases the diastereoselectivity was very good (>90:10 *anti*/*syn*). The presence of the Lewis acid was found to be pivotal in determining the stereochemical outcome of these reactions. Strongly chelating $TiCl_4$ led largely to the *anti* diastereomer with BH_3·SMe_2 as reducing agent. We are currently expanding the study of this reducing methodology.

(12) (a) Marcantoni, E.; Alessandrini, S.; Malavolta, M.; Bartoli, G.; Bellucci, M. C.; Sambri, L.; Dalpozzo, R. *J. Org. Chem.* **1999**, *64*, 1986−1992. (b) Marcantoni, E.; Cingolani, S.; Bartoli, G.; Bosco, M.; Sambri, L. *J. Org. Chem.* **1998**, *63*, 3624−3630.

(13) (a) Sarko, C. R.; Collibee, S. E.; Knorr, A. L.; Di Mare, M. *J. Org. Chem.* **1996**, *61*, 868−873. (b) Brown, H. C.; Kanth, J. V. B.; Dalvi, P. V.; Zaidlewicz, H. *J. Org. Chem.* **1999**, *64*, 6236−6274, and references therein.

(14) Normally, *J anti* < *J syn*: Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* **1982**, *65*, 1101−1133.

(15) Ballini, R.; Bartoli, G.; Gariboldi, P. V.; Marcantoni, E.; Petrini, M. *J. Org. Chem.* **1993**, *58*, 3368−3372.

(16) Kingsbury, C. A.; Sopchik, A. E.; Underwood, G.; Rajan, S. *J. Chem. Soc., Perkin Trans. 2* **1982**, 867−874.

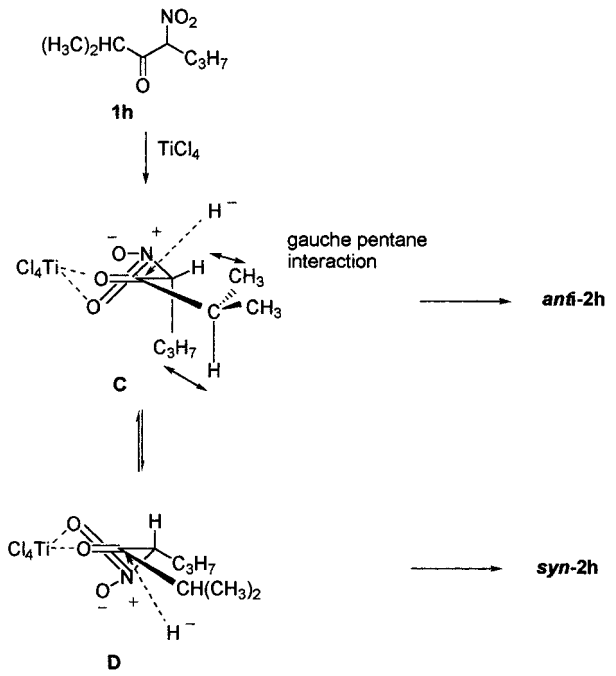
(17) Kessler, H.; Griesinger, C.; Kerrsenbaum, R.; Wagner, K.; Ernst, R. R. *J. Am. Chem. Soc.* **1987**, *109*, 607−609.

(18) Dalling, D. K.; Grant, D. M.; Johnson, L. F. *J. Am. Chem. Soc.* **1971**, *93*, 3678−3682.

(19) Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1998**, *63*, 9125−9127.

(20) (a) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151−4157. (b) Gennari, C.; Vieth, S.; Comotti, A.; Vulpetti, A.; Goodman, J. M.; Paterson, I. *Tetrahedron* **1992**, *48*, 4439−4458. (c) Bernardi, A.; Gennari, C.; Goodman, J. M.; Paterson, I. *Tetrahedron: Asymmetry* **1995**, *6*, 2613−2636. (d) Esteve, C.; Ferrero, M.; Romea, P.; Urpì, F.; Vilarrasa, J. *Tetrahedron Lett.* **1999**, *40*, 5079−5082.

Scheme 3



Experimental Section

To a cold solution (−78 °C) of α-nitro ketone **1** (1.0 mmol) in 10 mL of dry CH_2Cl_2 was added $TiCl_4$ (1.5 mmol) to give immediately a clear yellow solution, which was stirred for 15 min at this temperature. The complex BH_3·SMe_2 (1.5 mmol) in 5 mL of CH_2Cl_2 was then added. After 15 min, 25 mL of 1 N HCl was added, and the reaction was warmed to room temperature. The organic layer was separated, the aqueous layer was washed with CH_2Cl_2, and the combined organics were concentrated in vacuo. The resulting residue was partitioned between Et_2O and H_2O. The etheral layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The crude nitro alcohol **2**, obtained as a diastereomeric mixture of *syn* and *anti* product, was purified, if necessary, by flash cromatography (EtOAc/hexane = 2:8). The *syn*/*anti* ratios were determined by NMR spectroscopy.

2-Nitro-1-phenylheptan-1-ol (2a). *Anti* diastereomer: IR (neat) 3614, 3570, 1605, 1551, 1379 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74−0.93 (m, 3H), 1.1−1.4 (m, 6H), 1.72−1.91 (m, 1H), 2.01−2.3 (m, 1H), 2.75 (bs, 1H), 4.6−4.72 (ddd, J = 3.17, 4.84 and 10.86 Hz, 1H), 5.18 (d, J = 4.8 Hz, 1H), 7.3−7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.35, 22.74, 25.99, 28.17, 31.52, 74.74, 93.72, 126.65, 129.19, 129.25, 138.95; EI-MS *m*/*z* 190 (M − HNO_2), 133, 107 (100), 105, 77. Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.8; H, 8.07; N, 5.9. Found: C, 65.4; H, 8.02; N, 6.02.

2-Methyl-3-nitrooctan-4-ol (2b). *Anti* diastereomer: IR (neat) 3436, 1547, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 7.2 Hz, 3H), 0.97−1.18 (m, 6H), 1.20−1.58 (m, 6H), 1.98 (s, 1H), 2.33−2.45 (m, 1H), 4.0−4.08 (m, 1H), 4.33 (dd, J = 5.9 and 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.93, 18.35, 19.56, 22.41, 27.86, 28.36, 32.39, 70.44, 97.40; EI-MS *m*/*z* 142 (M − HNO_2), 127, 100, 85, 69, 57, 56 (100). Anal. Calcd for $C_9H_{19}NO_3$: C, 57.12; H, 10.12; N, 7.40. Found: C, 56.84; H, 10.26; N, 7.12. ***Syn* diastereomer:** IR (neat) 3436, 1547, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 7.2 Hz, 3H), 0.97−1.18 (m, 6H), 1.20−1.58 (m, 6H), 1.98 (s, 1H), 2.33−2.45 (m, 1H), 4.0−4.08 (m, 1H), 4.17 (dd, J = 4.15 and 9.12 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.93, 18.80, 18.97, 22.41, 27.85, 28.38, 32.45, 69.52, 98.2; EI-MS *m*/*z* 160, 143, 127, 100, 85, 69, 57, 56 (100). Anal. Calcd for $C_9H_{19}NO_3$: C, 57.12; H, 10.12; N, 7.40. Found: C, 56.84; H, 10.26; N, 7.12.

2-Nitro-1-(4-nitrophenyl)propan-1-ol (2c). *Anti* diastereomer: IR (Nujol) 3477, 1605, 1548, 1519, 1389, 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5 (d, J = 6.9 Hz, 3H), 2.9 (bs, 1H), 4.64−4.8 (dq, J = 3.2 and 6.9 Hz, 1H), 5.56 (d, J = 3.2 Hz, 1H), 7.6 (d, 2H), 8.4 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 11.86, 72.73, 86.78, 123.62, 124.12, 126.99, 131.20; EI-MS *m*/*z* 151 (100), 150, 77. Anal. Calcd for $C_9H_{10}N_2O_5$: C, 47.79; H, 4.46; N, 12.38. Found: C, 47.85; H, 4.40; N, 12.02. ***Syn* diastereomer:** IR (Nujol) 3477, 1605, 1548, 1519, 1389, 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4 (d, J = 6.9 Hz, 3H), 2.9 (bs, 1H), 4.26−4.34 (m, 1H), 5.2 (d, J = 8.8 Hz, 1H), 7.6 (d, 2H), 8.4 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 16.24, 74.91, 87.73, 123.62, 123.96, 127.88, 131.20; EI-MS *m*/*z* 151 (100), 150, 77. Anal. Calcd for $C_9H_{10}N_2O_5$: C, 47.79; H, 4.46; N, 12.38. Found: C, 47.85; H, 4.40; N, 12.02.

4-Nitro-1-phenylpentan-3-ol (2d). *Anti* diastereomer: IR (neat) 3435, 1602, 1546, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (d, J = 6.76 Hz, 3H), 1.7−1.95 (m, 2H), 2.3 (bs, 1H), 2.64−3.0 (m, 2H), 3.85−3.96 (ddd, J = 3.7, 6.96 and 8.99 Hz, 1H), 4.44−4.63 (dq, J = 6.79 and 6.79 Hz, 1H), 7.18−7.4 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.24, 31.44, 34.69, 71.95, 87.77, 126.28, 128.45, 128.63, 40.86; EI-MS *m*/*z* 162 (M − HNO_2), 145, 105, 91 (100), 57. Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.85; H, 7.40; N, 6.52. ***Syn* diastereomer:** IR (neat) 3435, 1602, 1546, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (d, J = 6.88 Hz, 3H), 1.7−1.95 (m, 2H), 2.3 (bs, 1H), 2.64−3.0 (m, 2H), 4.15−4.24 (dt, J = 3.5 and 9.24 Hz, 1H), 4.44−4.63 (dq, J = 6.79 and 6.79 Hz, 1H), 7.18−7.4 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 12.51, 31.92, 34.56, 71.03, 86.39, 126.28, 128.45, 128.63, 140.86; EI-MS *m*/*z* 162 (M − HNO_2), 145, 105, 91 (100), 57. Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.85; H, 7.40; N, 6.52.

2-Methyl-4-nitrotridecan-5-ol (2e). *Anti* diastereomer: IR (neat) 3434, 1549 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92−0.95 (m, 3H), 0.95−1.0 (m, 6H), 1.2−1.38 (m, 10H), 1.4−1.61 (m, 4H), 2.0−2.4 (m, 3H), 3.94−4.02 (m, 1H), 4.51−4.58 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.09, 21.19, 22.64, 23.16, 25.8, 25.62, 29.18, 29.36, 31.80, 33.06, 36.60, 39.32, 72.52, 90.45; EI-MS *m*/*z* 213 (M − NO_2), 169, 141, 99, 57, 43 (100). Anal. Calcd for $C_{14}H_{29}NO_3$: C, 64.83; H, 11.27; N, 5.4. Found: C, 63.95; H, 11.30; N, 5.32. ***Syn* diastereomer:** IR (neat) 3434, 1549 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92−0.95 (m, 3H), 0.95−1.0 (m, 6H), 1.2−1.38 (m, 10H), 1.4−1.61 (m, 4H), 2.0−2.4 (m, 3H), 3.78−3.83 (m, 1H), 4.48−4.51 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.09, 21.31, 22.64, 23.01, 25.26, 25.62, 29.30, 29.40, 31.80, 33.65, 36.60, 39.32, 72.37, 91.14; EI-MS *m*/*z* 213 (M − NO_2), 169, 141, 99, 57, 43 (100). Anal. Calcd for $C_{14}H_{29}NO_3$: C, 64.83; H, 11.27; N, 5.4. Found: C, 63.95; H, 11.30; N, 5.32.

6-Nitrooctadecan-7-ol (2f). *Anti* diastereomer: IR (neat) 3435, 1550, 1378 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83−0.9 (m, 6H), 1.2−1.35 (m, 24H), 1.4−1.58 (m, 3H), 1.68−1.72 (m, 1H), 1.98−2.18 (m, 1H), 3.95−4.02 (m, 1H), 4.38−4.47 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.89, 14.12, 22.30, 22.68, 25.28, 25.36, 25.64, 27.88, 29.09, 29.30, 29.32, 29.45, 29.60, 31.08, 31.15, 33.18, 72.38, 92.35; EI-MS *m*/*z* 269 (M − NO_2), 183, 140, 113, 70, 55 (100). Anal. Calcd for $C_{18}H_{37}NO_3$: C, 68.53; H, 11.82; N, 4.44. Found: C, 68.75; H, 11.30; N, 4.46. ***Syn* diastereomer:** IR (neat) 3435, 1550, 1378 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83−0.9 (m, 6H), 1.2−1.35 (m, 24H), 1.4−1.58 (m, 3H), 1.68−1.72 (m, 1H), 1.98−2.18 (m, 1H), 3.8−3.88 (m, 1H), 4.38−4.47 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.89, 14.12, 22.30, 22.68, 25.28, 25.36, 25.64, 27.88, 29.09, 29.30, 29.32, 29.45, 29.52, 30.45, 31.90, 33.62, 72.06, 92.88; EI-MS *m*/*z* 269 (M − NO_2), 183, 140, 113, 70, 55 (100). Anal. Calcd for $C_{18}H_{37}NO_3$: C, 68.53; H, 11.82; N, 4.44. Found: C, 68.75; H, 11.30; N, 4.46.

2-Nitro-1-phenylpentan-3-ol (2g). *Anti* diastereomer: IR (neat) 3435, 1605, 1548, 1376 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (t, J = 7.35 Hz, 3H), 1.45−1.62 (m, 2H), 3.15−3.35 (m, 2H), 3.9−3.98 (ddd, J = 5.17, 5.17 and 10.38 Hz, 1H), 4.0 (bs, 1H), 4.6−4.72 (m, 1H), 7.1−7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 10.00, 26.48, 34.60, 73.43, 93.63, 127.16, 128.74, 128.81, 136.2; EI-MS *m*/*z* 162 (M − HNO_2), 145, 133, 105, 91 (100), 77, 57. Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.35; H, 7.30; N, 6.56. ***Syn* diastereomer:** IR (neat) 3435, 1605, 1548, 1376 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (t, J = 7.35 Hz, 3H), 1.45−1.62 (m, 2H), 3.15−3.35 (m, 2H), 3.75−3.86 (ddd, J = 4.11, 5.94 and 10.25 Hz, 1H), 4.0 (bs, 1H), 4.6−4.72 (m, 1H), 7.1−7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 9.74, 26.62, 36.37, 72.67, 93.68, 127.37, 128.74, 128.81, 135.4; EI-MS *m*/*z* 162 (M − HNO_2), 145, 133, 105, 91 (100), 77, 57. Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.35; H, 7.30; N, 6.56.

2-Methyl-4-nitroheptan-3-ol (2h). *Anti* diastereomer: IR (neat) 3468, 1551, 1377 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, J =

6.7 Hz, 3H), 1.0 (d, J = 6.7 Hz, 6H), 1.28−1.42 (m, 2H), 1.62−1.82 (m, 2H), 2.0 (bs, 1H), 1.88−2.18 (m, 1H), 3.6 (dd, J = 5.4 and 6.6 Hz, 1H), 4.52−4.64 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.39, 16.25, 19.16, 19.68, 29.95, 32.55, 77.12, 90.74; EI-MS m/z 146 (M − Et), 132 (M − ^{i}Pr), 128 (M − HNO_2), 99, 86, 85, 71, 57, 43 (100). Anal. Calcd for $C_8H_{17}NO_3$: C, 54.84; H, 9.78; N, 7.99. Found: C, 54.90; H, 9.30; N, 7.66. ***Syn* diastereomer:** IR (neat) 3468, 1551, 1377 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (t, J = 6.7 Hz, 3H), 0.94 (d, J = 6.7 Hz, 6H), 1.28−1.42 (m, 2H), 1.62−1.82 (m, 2H), 2.0 (bs, 1H), 1.88−2.18 (m, 1H), 3.73 (dd, J = 4.57 and 6.4 Hz, 1H), 4.52−4.64 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.47, 17.48, 19.01, 19.26, 30.44, 30.52, 76.54, 90.05; EI-MS m/z 146 (M − Et), 132 (M − ^{i}Pr), 128 (M − HNO_2), 99, 86, 85, 71, 57, 43 (100). Anal. Calcd for $C_8H_{17}NO_3$: C, 54.84; H, 9.78; N, 7.99. Found: C, 54.90; H, 9.30; N, 7.66.

1-Cyclohexyl-2-nitrohexan-1-ol (2i). *Anti* diastereomer: IR (neat) 3436, 1548, 1368 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8−1.0 (m, 3H), 1.05−1.45 (m, 10H), 1.5−1.9 (m, 6H), 1.9−2.3 (m, 1H), 3.6 (bs, 1H), 3.58 (t, J = 5.84 Hz, 1H), 4.52−4.71 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.23, 22.58, 26.15, 26.49, 26.58, 28.29, 28.60, 30.30, 30.86, 40.82, 70.57, 90.49; EI-MS m/z 212 (M − OH), 182 (M − HNO_2), 165, 111, 99, 83, 55 (100). Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 61.90; H, 10.30; N, 6.64. ***Syn* diastereomer:** IR (neat) 3436, 1548, 1368 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8−1.0 (m, 3H), 1.05−1.45 (m, 10H), 1.5−1.9 (m, 6H), 1.9−2.3 (m, 1H), 3.6 (bs, 1H), 3.78 (dd, J = 4.28 and 6.64 Hz, 1H), 4.52−4.71 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.23, 22.68, 26.24, 26.39, 27.45, 27.92, 28.54, 29.76, 30.86, 40.62, 76.57, 90.80; EI-MS m/z 212 (M − OH), 182 (M − HNO_2), 165, 111, 99, 83, 55 (100). Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 61.90; H, 10.30; N, 6.64.

Acknowledgment. This work has been carried out in the frame of the National Project “Stereoselezione in Sintesi Organica. Metodologie e Applicazioni” by the Ministry of University and Technological Research (MURST) Rome and by the University of Camerino. The authors thank Dr. Gianni Rafaiani for his help in the NMR experiments, also.

JO000542Z