Reactivity of α-Nitro Ketones toward Organometallic Reagents: Straightforward Synthesis of Tertiary β-Nitroalkanols

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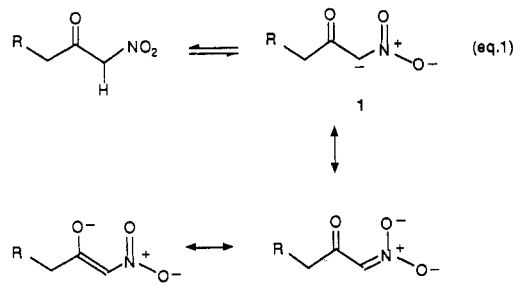
Tertiary β-nitro alcohols can be efficiently obtained from the reaction of α-nitro ketones with 2 equiv of an organomagnesium or organolithium reagent. Unexpectedly, Grignard reagents do not deprotonate the α acidic proton of **2** but instead strongly coordinate with the carbonyl and the nitro oxygens. A second equivalent of reagent is thus necessary to carry out the addition. Magnesium reagents fail to react with open-chain α-nitro ketones because a rapid deprotonation occurs, and Grignard reagents are unable to attack monoanion **1**. Organolithiums are stronger nucleophiles than organomagnesium reagents and can attack deprotonated substrates. The diastereoselectivity of the reaction depends on the reagent used. Grignard reagents produced almost exclusively *trans* nitroalkanols with **2**, whereas organolithiums show little or no selectivity with the same substrate. Conversely, lithium reagents show excellent stereoselectivity with open-chain substrates and affords the *anti* diastereomer.

Introduction

The remarkable synthetic potential of α-nitro ketones has been revealed by a considerable number of studies which have shown their reactivity and great versatility.[1] The juxtaposition of the carbonyl carbon and the carbon bearing the nitro group offers flexible reactivity patterns that are peculiar to this class of compounds. The removal of the hydrogen atom in the α position allows the easy formation of a doubly stabilized carbanion which is a powerful reagent for efficient carbon–carbon bond formation (eq 1).[2] Alkylation in the α′ position requires the



generation of a dianion, which undergoes attack at the most basic enolate site.[3] Unfortunately, this doubly deprotonated reagent possesses rather low nucleophilicity.[4] The low nucleophilicity can be enhanced by the use of the more reactive hydrazone or imine derivatives[5] or by the choice of an appropriate base/solvent combination to generate the dianion.[6]

Cyclic α-nitro ketones undergo facile ring cleavage at the bond between the carbonyl group and the nitro group by means of nucleophilic agents under mild conditions. This retro-Claisen process provides a useful synthesis of α,ω disubstituted compounds[7] and can be accomplished either in oxidative[8] or reductive[9] fashion. Reactions with internal nucleophiles present in the alkyl branch in the α position give macrocyclic compounds through a ring enlargement process.[10] The nitro group can also be directly replaced by hydrogen, and this process has greatly increased the synthetic potential of α-nitro ketones.[11] A tandem denitration–deoxygenation sequence, performed by reduction of *p*-tolylsulfonylhydrazones of α-nitro ketones, provides the corresponding alkanes in good yields.[12]

Rather surprisingly, no reports on the reactivity of α-nitro ketones with organometallic reagents have been found in the literature to date. This reaction would be of some importance in organic synthesis since it would produce tertiary β-nitro alcohols, a class of compounds difficult to obtain by direct nitroaldol condensation on ketones.[13] Reactions of simple nitroalkanes with alkyl and aryl Grignard reagents usually lead to complex mixtures of products in which the starting nitro compound, arising from a deprotonation reaction, and other redox products usually predominate.[14] In contrast, benzylic and allylic reagents chemoselectively attack the nitrogen atom, and further manipulation of the resulting intermediate

(1) Reviews: (a) Rosini, G.; Ballini, R.; Petrini, M.; Marotta, E.; Righi, P. *Org. Prep. Proc. Int.* **1990**, *22*, 707. (b) Fischer, R. H.; Weitz, H. M. *Synthesis* **1981**, 261.

(2) (a) Stach, H.; Hesse, M. *Helv. Chim. Acta* **1986**, *69*, 1614. (b) Ono, N.; Hamamoto, I.; Kaji, A. *J. Org. Chem.* **1986**, *51*, 2832. (c) Ognyanov, V. I.; Hesse, M. *Synthesis* **1985**, 645. (d) Ono, N.; Miyake, H.; Fuji, M.; Kaji, A. *Tetrahedron Lett.* **1983**, *24*, 3477. (e) Ono, N.; Miyake, H.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1983**, 875.

(3) Thompson, C. M.; Green, D. L. C. *Tetrahedron* **1991**, *47*, 4223.

(4) Dampawan, P.; Zajac, W. W. *J. Org. Chem.* **1982**, *47*, 1176.

(5) (a) Denmark, S. E.; Sternberg, J. A.; Lueoend, R. *J. Org. Chem.* **1988**, *53*, 1251. (b) Denmark, S. E.; Ares, J. J. *J. Am. Chem. Soc.* **1988**, *110*, 4432.

(6) Ballini, R.; Bartoli, G.; Castagnani, R.; Marcantoni, E.; Petrini, M. *Synlett* **1992**, 64.

(7) (a) Ballini, R.; Petrini, M. *Synth. Commun.* **1986**, *16*, 1781. (b) Aono, T.; Bieri, J. H.; Hesse, M.; Kostova, K.; Lorenzi-Riatsch, A.; Nakashita, Y.; Prewo, R. *Helv. Chim. Acta* **1985**, *68*, 1033.

(8) Ballini, R.; Marcantoni, E.; Petrini, M.; Rosini, G. *Synthesis* **1988**, 915.

(9) Ballini, R.; Petrini, M.; Rosini, G. *Tetrahedron* **1990**, *46*, 7531.

(10) Stach, H.; Hesse, M. *Tetrahedron* **1988**, *44*, 1573.

(11) For a review on this topic see: Ono, N.; Kaji, A. *Synthesis* **1986**, 693. For a more recent example: Kamimura, A.; Kurata, K.; Ono, N. *Tetrahedron Lett.* **1989**, *30*, 4819.

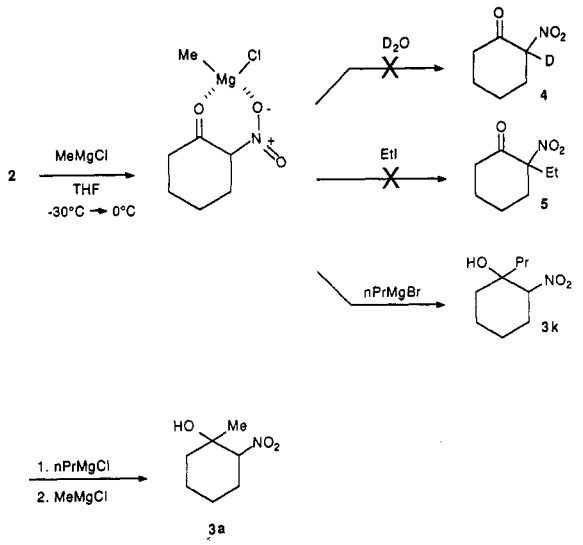
(12) Ballini, R.; Petrini, M.; Rosini, G. *J. Org. Chem.* **1990**, *55*, 5159.

(13) Seebach, D.; Lehr, F. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 505. Recently tertiary nitro alcohols have been prepared in fair to good yields (60–90%) by high pressure (9 kbar) reactions of cyclic ketones with nitroalkanes in the presence of Bu_4NF: Matsumoto, K. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 617.

(14) Bartoli, G.; Marcantoni, E.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 5834.

0022-3263/93/1958-3368$04.00/0

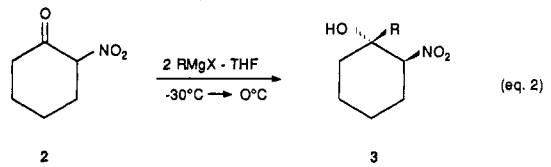
Scheme I



affords allyl hydroxylamines,[15] or nitrones,[14] depending on the quenching conditions selected.

Results and Discussion

The reactions of α-nitrocyclohexanone (**2**) with 2 equiv of Grignard reagents afforded the corresponding nitro alcohols **3** in good yields (eq 2). The first equivalent of

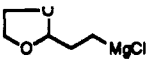
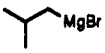


the reagent was initially believed to act as a base, with deprotonation leading to anion **1**, but some simple experiments to demonstrate its formation did not give any conclusive results. The reaction mixture obtained by treating **2** with MeMgCl was quenched with electrophiles such as D_2O and EtI, but no trace of **4** or addition product **5** was found in the mixture (Scheme I). Nevertheless, the addition of 1 equiv of a different Grignard reagent (i.e., *n*-PrMgCl) to this mixture afforded only nitro alcohol **3k**, arising from the second organomagnesium species, after the usual workup. When the order of the Grignard addition was reversed (1. *n*-PrMgCl, 2, MeMgCl), the formation of **3a** was exclusively observed.

The logical conclusion of these findings is that the Grignard reagent does not actually carry out any deprotonation but only coordinates, by the magnesium atom, the carbonyl and nitro oxygens. The chelation enhances the reactivity of the carbonyl group toward the second equivalent of RMgX, and this coordination must be faster than both the nucleophilic attack or any equilibrium exchange between Grignard species, as evidenced by the experiments cited above. In fact, an identical result was obtained when 1 equiv of $Et_2O{\cdot}MgBr_2$ was added to **2** prior to the addition of the reagent. Grignard addition was usually carried out at −30 °C, and then the mixture was allowed to warm up to 0 °C and held at this temperature for the appropriate time (Table I). It is worth noting that

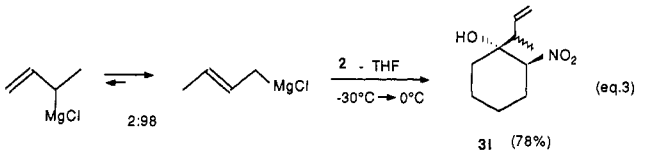
(15) Barboni, L.; Bartoli, G.; Marcantoni, E.; Petrini, M.; Dalpozzo, R. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2133.

Table I. Reactions of 2-Nitrocyclohexanone (2) with Grignard Reagents

entry	RMgX	product 3	reaction[a] time (h)	yield[b] (%)
1	MeMgCl	**a**	0.5	66
2	EtMgBr	**b**	0.5	83
3	*n*-BuMgBr	**c**	1.0	70
4	PhMgCl	**d**	1.5	78
5		**e**	1.0	77
6		**f**	1.5	70
7		**g**	1.5	60
8	PhC≡CMgCl	**h**	1.5	78
9	$PhCH_2MgCl$	**i**	1.0	80
10	CH_2=C=CHMgBr	**j**	1.5	85

[a] Stirring time at 0 °C. [b] Yields of pure, isolated products.

only primary Grignard reagents can be efficiently introduced. Secondary Grignards do not give any reaction: the substrate is almost completely recovered after the mixture is quenched. Allenylmagnesium reagents are known to lead mainly to acetylene adducts with carbonyl compounds,[16] but, in our process, only the allenic β-nitro alcohol **3j** is produced. The behavior displayed by 2-butenylmagnesium chloride is interesting: although in the equilibrium mixture of the reagent, the primary form largely prevails over the secondary,[17] only the product (**3l**) arising from the latter form is obtained as a diastereomeric mixture (eq 3). This method represents the only way by which a secondary group can be introduced.



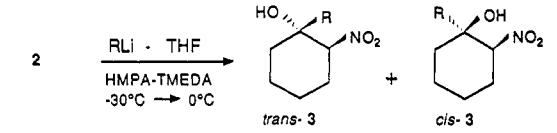
This Grignard reaction also shows surprising stereoselectivity: *trans* isomers **3** are exclusively formed. The stereochemical outcome of this reaction can be rationalized by invoking Mg atom chelation that produces a bicyclic locked structure in which the 2,6 axial hydrogens strongly favor the approach of the nucleophile on the side of the molecule opposite the two hydrogens. This approach leads to the selective formation of the *trans* isomer. The stereochemistries of these products were established by ^{1}H-NMR spectroscopy and by measurement of the intramolecular NOE effect between the C2H and the OH protons. The experiments were carried out in DMSO, a solvent which is known to inhibit proton exchange. The inhibition of proton exchange makes the peaks for the hydroxy protons sharper. Usually C2H is found in the axial position[4] (compound **3a** 2H: δ 4.46, J_{aa} = 11.6Hz), and saturation of C2H causes a strong NOE on the hydroxyl proton. Conversely, saturation of the OH results in an increase of the C2H signal and of course the methyl signals.

Organolithium reagents lead to similar results, but the use of HMPA (or DMPU) as a cosolvent and TMEDA as a lithium chelating agent is necessary to ensure good results (Table II). Unlike the Grignard reagents, organolithiums

(16) Suzuki, M.; Morita, Y.; Noyori, R. *J. Org. Chem.* **1990**, *55*, 441 and references cited therein.

(17) Hutchinson, D. A.; Beck, K. R.; Benkeser, R. A.; Grutzner, J. B. *J. Am. Chem. Soc.* **1973**, *95*, 7075.

Table II. Reactions of 2-Nitrocyclohexanone (2) with Organolithium Reagents



entry	R	product[a] 3	cis–trans ratio	reaction time (h)	yield (%)
1	Me	**a**	0/100	2.5	83
2	n-Bu	**c**	33/67	3.0	80
3		**m**	25/75	3.5	88
4		**e**	14/86	3.0	77

[a] Yield of pure, isolated products.

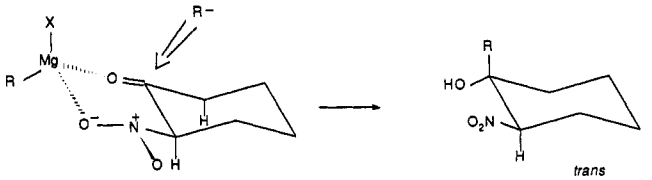


Figure 1. Proposed model for the stereoselective attack of the Grignard reagent on **2**.

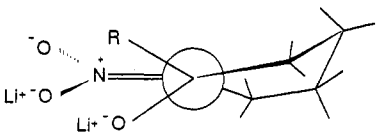
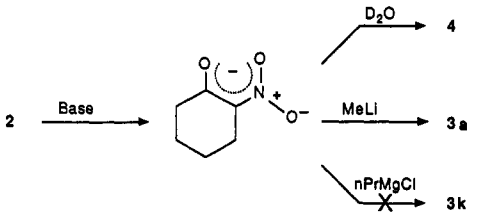


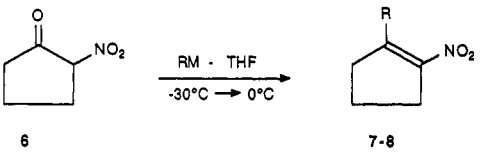
Figure 2. Conformation of the intermediate lithium dianion.

Scheme II



are able to deprotonate the nitro ketone, under these conditions, to give the corresponding monoanion. However, lithium reagents are strong enough nucleophiles to further attack the monoanion, whereas the less reactive RMgX reagents are unable to do so. Some experiments carried out with the monoanion of **2**, generated using different bases, clearly show this behavior (Scheme II). Although RLi reagents give better chemical yields than do the RMgX reagents, a lower degree of diastereoselectivity is generally observed with the lithium reagents. The lower selectivity is not surprising because the final stereochemistry of the products is governed by the stereochemistry of the protonation of the nitronate anion that is formed upon RLi attack (Figure 2). Addition of HMPA usually results in a suppression of the chelation aptitude of metals,[18] and the repulsion between the negatively charged oxygen atoms brings about a distortion in the normal chair conformation of the ring. This distortion makes the two sides almost equally approachable

Scheme III

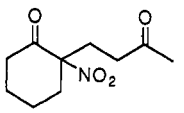


ENTRY	RM	PRODUCT	YIELD(%)
1	MeMgCl	7	90
2	MeLi	7	75
3	nPrMgCl	8	78

by the quenching source and causes the reduction in diastereoselectivity. The high selectivity observed for MeLi is quite surprising, and no explanation has been found.

The success of this procedure strongly depends on the ring size of the substrate. α-Nitrocyclopentanone (**6**) reacts with RMgX as well as with RLi, but the intermediate nitroalkanol presumably formed suffers a rapid elimination giving the corresponding nitro alkenes **7–8** in good yields (Scheme III).[19] All attempts to trap the intermediate nitro alcohol were unsuccessful; only decomposition products were obtained. This unexpected result is certainly not uninteresting since nitroolefins are valuable intermediates in organic chemistry.[20]

The presence in the substrate of other electrophilic functionalities very often curtails the usefulness of this reaction. As an example, compound **9** produces only complex mixtures of products when treated with RMgX or RLi reagents even under carefully controlled conditions.



9

Open-chain α-nitro ketones cannot be converted into the corresponding alkanols by means of RMgX reagents. The deprotonation of the α hydrogen occurs more readily in linear frameworks, and the second equivalent of the reagent is unable to attack the monoanion in a profitable way. Products arising from a retro-Claisen reaction of the substrate have sometimes been recovered.[21] Conversely, RLi reagents display remarkable reactivity, even with 2-nitro-3-pentanone (**10**), and afford the corresponding nitroalkanols **11** in good yields (Table III). A high degree of diastereoselectivity is also observed in this reaction: the *anti* nitro alcohols are formed exclusively, except when MeLi is employed.

A possible explanation for these stereochemical outcomes is the participation of the conformation, already proposed by Seebach, for the intermediate nitronate

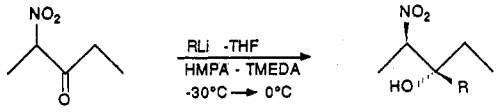
(18) Huryn, D. M. Carbanions of Alkali and Alkaline Earth Cations: Selectivity of Carbonyl Addition Reactions. In *Comprehensive Organic Synthesis*; Schreiber, S. L., Ed.; Pergamon Press: Oxford, 1991; Vol. 1, p 49.

(19) Dampawan, P.; Zajac, W. W. *Tetrahedron Lett.* **1982**, *23*, 135.

(20) For general reviews on nitroalkene synthesis see: (a) Barrett, A. G. M.; Graboski, G. G. *Chem. Rev.* **1986**, *86*, 751. (b) Kabalka, G. W.; Varma, R. S. *Org. Prep. Proc. Int.* **1987**, *19*, 285.

(21) For instance, the reaction of **10** with *n*-decylmagnesium bromide affords 3-tridecanone in 38% yield.

Table III. Reactions of 2-Nitro-3-pentanone (10) with Organolithium Reagents

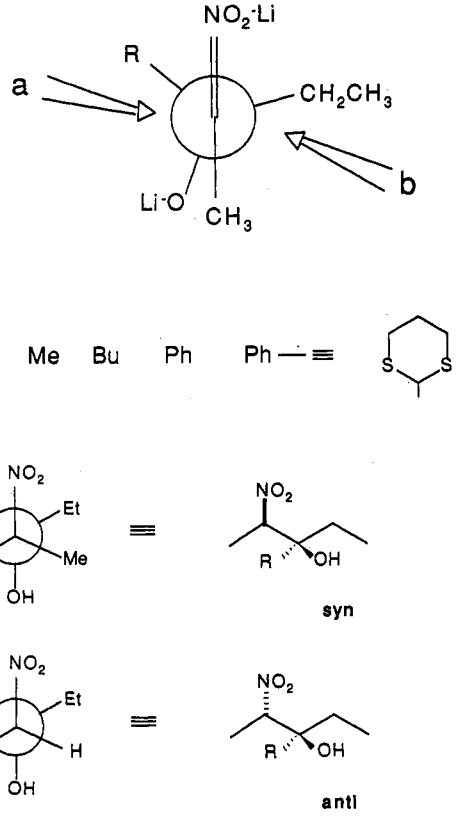


10 anti 11

entry	R	product 11	reaction time (h)	yield[a] (%)
1	Me	a[b]	1.5	78
2	*n*-Bu	b	2.5	92
3	Ph	c	3.0	85
4		d	3.0	87
5	PhC≡C—	e	3.5	90

[a] Yields of pure, isolated products. [b] A 3:2 syn/anti mixture is recovered.

Scheme IV



anion.[22] In that conformation, the negatively charged oxygens are forced to assume the *anti* position because of the electronic repulsion (Scheme IV). The introduction of larger groups forces the proton source to enter from the ethyl side (b) to afford the *anti* isomer. The methyl group is unable to exert a consistent degree of differentiation between the two faces, and thus only modest diastereoselectivity is observed for compound **11b**.

The assignments of the structures for compounds 11 were made by ^{1}H-NMR spectroscopy. It was assumed that a hydrogen bond between the nitro group and the OH locks the structure in a semirigid conformation.[23] Indeed, no concentration effects were observed either in the IR absorptions or in the proton chemical shift values for the OH signals. Compound **11c** was submitted to a ROESY analysis,[24] and no interesting cross-peaks were detected at rt with mixing times ranging from 0.8 to 1.2 s. At −20 °C, besides the expected ROE effects between the C3H and C4H, interesting cross-peaks appeared between C2H and the aromatic ring protons and between C2H and one of the C3H. These cross-peaks demonstrate that, in compound **11c**, in the presence of hydrogen bonding, C2H and the aromatic ring are in close proximity, as would be expected for an *anti* configuration of the molecule.

In conclusion, a new synthesis of tertiary nitroalkanols has been realized. The present methodology is simple and reliable, and it complements the direct nitroaldol condensation. The process also shows considerable diastereoselectivity, depending on the nature of the organometallic compounds employed.

Experimental Section

^{1}H-NMR spectra were recorded at 300 MHz in $CDCl_3$. *J* values are given in Hz. ROESY experiments were run in a 10^{-2} M $CDCl_3$ solution. A time-shared spin lock pulse was used. Data points were collected in two matrixes of 1024 × 1024; 256 increments were used with 16 transients each; mixing time was 0.8 s; the spectral window was 2400 Hz in both dimensions. Mass spectra were obtained by means of the EI technique. Reaction progress was monitored by TLC or capillary GC. Melting points are uncorrected. Flash chromatography[25] was performed on Merck silica gel (0.040–0.063 mm) with hexane–ethyl acetate (7:3) as the eluent. All chemicals used were commercial, and literature methods were followed for the synthesis of 2-nitro-3-pentanone (**10**)[26] and organometallic reagents. THF was dried by refluxing it over sodium wire until the blue color of benzophenone ketyl persisted and distilling it into a dry receiver under a nitrogen atmosphere. HMPA and DMPU were dried by distillation from CaH_2 and were stored over 4A molecular sieves.

Reaction between α-Nitrocyclohexanone (2) and Grignard Reagents. 1-Methyl-2-nitrocyclohexanol (3). To a stirred THF solution (40 mL) of α-nitrocyclohexanone (**2**) (0.715 g, 5 mmol) at −30 °C was added methylmagnesium chloride (11 mmol, 4.40 mL, 2.5 M in THF) under N_2. The mixture was stirred for 20 min, and then the temperature was raised to 0 °C, and stirring was continued for an additional 30 min. The mixture was then quenched with saturated aqueous NH_4Cl, extracted with ether, and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the crude product was submitted to a flash chromatographic purification (hexane–ethyl acetate (7:3)) affording 0.525 g (66%) of nitro alcohol **3a** as a white solid: mp 68 °C (from hexane); IR (cm^{-1}, KBr) 3200 (OH), 1520 (NO_2); ^{1}H-NMR δ 1.20 (3H, s), 1.25–1.40 (2H, m), 1.50–1.70 (2H, m), 1.80–2.00 (3H, m), 2.10–2.20 (1H, m), 3.15 (1H, s, OH), 4.43 (1H, dd, *J* = 11.6, 4.6, $CHNO_2$); MS *m/z* 144, 113, 98, 95, 83, 70, 55, 43. Anal. Calcd for $C_7H_{13}NO_3$ (159.19): C, 52.81; H, 8.23; N, 8.80. Found: C, 52.79; H, 8.25; N, 8.79.

1-Ethyl-2-nitrocyclohexanol (3b): yield 83%; oil; IR (cm^{-1}, neat) 3400 (OH), 1530 (NO_2); ^{1}H-NMR δ 0.95 (3H, t, *J* = 7.0), 1.15–1.40 (4H, m), 1.50–2.20 (6H, m), 2.95 (1 H, s, OH), 4.45 (1H, dd, *J* = 11.7, 4.4, $CHNO_2$); MS *m/z* 144, 127, 109, 98, 83, 70, 57, 55, 43. Anal. Calcd for $C_8H_{15}NO_3$ (173.21): C, 55.47; H, 8.73; N, 8.08. Found: C, 55.49; H, 8.77; N, 8.13.

1-Butyl-2-nitrocyclohexanol (3c): yield 70%; oil; IR (cm^{-1}, neat) 3400 (OH), 1530 (NO_2); ^{1}H-NMR δ 0.90 (3H, t, *J* = 6.8), 1.05–1.45 (7H m), 1.60–1.80 (2H, m), 1.85–2.20 (5H, m), 3.00 (1H, s, OH), 4.46 (1H, dd, *J* = 11.7, 4.4, $CHNO_2$); MS *m/z* 184, 183,

(22) (a) Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* **1982**, *65*, 1101. (b) Seebach, D.; Eyer, M. *J. Am. Chem. Soc.* **1985**, *107*, 3601.

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

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

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(26) Rosini, G.; Ballini, R.; Sorrenti, P.; Petrini, M. *Synthesis* **1984**, 607.

144, 113, 98, 83, 70, 69, 55, 43. Anal. Calcd for $C_{10}H_{19}NO_3$ (201.27): C, 59.67; H, 9.51; N, 6.96. Found: C, 59.66; H, 9.53; N, 6.94.

1-Phenyl-2-nitrocyclohexanol (3d): yield 78%; mp 93 °C (from hexane); IR (cm^{-1}, KBr), 3500 (OH), 1530 (NO_2); ^{1}H-NMR δ 1.60–1.80 (4H, m), 2.20–2.45 (3H + 1H (OH), m), 2.75–2.82 (1H, m), 4.83 (1H, dd, J = 11.6, 4.4, $CHNO_2$), 7.20–7.30 (3H, m), 7.45–7.50 (2H, m); MS mz 221 (M^+), 203, 186, 173, 105, 91, 77, 70, 55, 41. Anal. Calcd for $C_{12}H_{15}NO_3$ (221.26): C, 65.14; H, 6.83; N, 6.33. Found: C, 65.16; H, 6.82; N, 6.25.

1-Vinyl-2-nitrocyclohexanol (3e): yield 77%; oil; IR (cm^{-1}, neat) 3480 (OH), 1530 (NO_2); ^{1}H-NMR δ 1.30–1.45 (2H, m), 1.60–1.75 (2H, m), 1.80–2.05 (3H, m), 2.20–2.30 (1H, m), 3.45 (1H, s, OH), 4.48 (1H, dd, J = 11.7, 4.4, $CHNO_2$), 5.27 (1H, dd, J = 10.8, 1.1, $=CHH_b$), 5.47 (1H, dd, J = 17.0, 1.1, $=CHH_a$), 6.18 (1H, dd, J = 17.1, 10.8, $CH_x=$); MS m/z 154, 136, 98, 83, 70, 55, 43. Anal. Calcd for $C_8H_{13}NO_3$ (171.20): C, 56.12; H, 7.65; N, 8.18. Found: C, 56.10; H, 7.61; N, 8.15.

1-(1,3-Dioxolan-2-ylethyl)-2-nitrocyclohexanol (3f): yield 70%; oil; IR (cm^{-1}, neat) 3370 (OH), 1520 (NO_2); ^{1}H-NMR δ 1.20–1.50 (4H, m), 1.60–2.10 (7H, m), 2.15–2.25 (1H, m), 3.55 (1H, s, OH), 3.80–4.00 (4H, m), 4.48 (1H, dd, J = 10.8, 4.4, $CHNO_2$), 4.87 (1H, t, J = 4.1, OCHO); MS m/z 244, 2.28, 198, 144, 129, 73, 57, 55, 43. Anal. Calcd for $C_{11}H_{19}NO_5$ (245.28): C, 53.86; H, 7.80; N, 5.71. Found: C, 53.83; H, 7.77; N, 5.70.

1-(2-Methylpropyl)-2-nitrocyclohexanol (3g): yield 60%; mp 78 °C (from hexane); IR (cm^{-1}, KBr) 3390 (OH), 1530 (NO_2); ^{1}H-NMR δ 0.95 (6H, d, J = 7.0), 1.20–1.35 (3H, m), 1.60–1.70 (2H, m), 1.80–2.05 (3H, m), 2.10–2.15 (1H, m), 3.00 (1H, s, OH), 3.82 (2H, d, J = 7.0), 4.38 (1H, dd, J = 11.6, 4.4, $CHNO_2$); MS m/z 183, 171, 155, 109, 98, 83, 57, 55, 43. Anal. Calcd for $C_{10}H_{19}NO_3$ (201.27): C, 59.67; H, 9.51; N, 6.96. Found: C, 59.65; H, 9.53; N, 6.98.

1-(Phenylethynyl)-2-nitrocyclohexanol (3h): yield 78%; mp 105 °C (from hexane); IR (cm^{-1}, KBr) 3480 (OH), 2200 (C–C triple bond), 1530 (NO_2); ^{1}H-NMR δ 1.30–1.40 (2H, m), 1.60–1.80 (3H, m), 2.00–2.10 (2H, m), 2.30–2.42 (1H, m), 3.60 (1H, s, OH), 4.41 (1H, dd, J = 11.7, 4.4, $CHNO_2$), 7.25–7.32 (3H, m), 7.40–7.46 (2H, m); MS m/z 245 (M^+), 228, 199, 153, 136, 98, 77, 70, 65, 55, 43. Anal. Calcd for $C_{14}H_{15}NO_3$ (245.28): C, 68.55; H, 6.16; N, 5.71. Found: C, 68.52; H, 6.18; N, 5.72.

1-(Phenylmethyl)-2-nitrocyclohexanol (3i): yield 80%; mp 109 °C (from hexane); IR (cm^{-1}, KBr) 3500 (OH), 1530 (NO_2); ^{1}H-NMR δ 1.20–2.00 (6H, m), 2.05–2.30 (2H, m), 2.50 (2H, s), 2.70 (1H, s, OH), 4.54 (1H, dd, J = 11.7, 4.4, $CHNO_2$), 7.20–7.40 (5H, m); MS m/z 235 (M^+), 217, 177, 144, 91, 80, 77, 65, 41. Anal. Calcd for $C_{13}H_{17}NO_3$ (235.28): C, 66.36; H, 7.28; N, 5.95. Found: C, 66.33; H, 7.24; N, 5.90.

1-Allenyl-2-nitrocyclohexanol (3j): yield 85%; oil; IR (cm^{-1}, neat) 3400 (OH), 1950 (C=C=C), 1530 (NO_2); ^{1}H-NMR δ 1.60–1.80 (4H, m), 2.20–2.40 (3H, m), 2.70–2.80 (1H, m), 3.35 (1H, s, OH), 4.49 (2H, d, J = 6.7), 4.84 (1H, dd, J = 11.7, 4.7, $CHNO_2$); MS m/z 154, 144, 111, 98, 83, 69, 55, 41. Anal. Calcd for $C_9H_{13}NO_3$ (183.21): C, 59.00; H, 7.15; N, 7.64. Found: C, 59.05; H, 7.15; N, 7.65.

1-(1-Methyl-2-propenyl)-2-nitrocyclohexanol (3l): yield 78%; oil; IR (cm^{-1}, neat) 3500 (OH), 1540 (NO_2); ^{1}H-NMR δ 1.05 (3H, d, J = 4.9), 1.30–1.55 (5H, m), 1.95–2.10 (2H, m), 2.40–2.50 (2H, m), 2.95 (1H, s, OH), 4.46 (1H, dd, J = 11.7, 4.4, $CHNO_2$), 5.05–5.10 (2H, m), 5.85–5.95 (1H, m); MS m/z 182, 157, 144, 108, 98, 83, 69, 55, 41, 39. Anal. Calcd for $C_{10}H_{17}NO_3$ (199.25): C, 60.28; H, 8.60; N, 7.03. Found: C, 60.27; H, 8.59; N, 7.05.

Reaction between α-Nitrocyclohexanone (2) and Lithium Reagents. 1-Allyl-2-nitrocyclohexanol (3m). To a stirred THF solution (40 mL) of α-nitrocyclohehanone (2) (0.715 g, 5 mmol) were added DMPU (8 mL) and TMEDA (1.06 g, 1.48 mL, 10.5 mmol). The solution was cooled to −30 °C, and then allyllithium (10.5 mmol, 5.52 mL, 1.9 M in THF) was added under N_2. The mixture was stirred for 20 min and then warmed to 0 °C; stirring was continued for an additional 3.5 h. The mixture was then quenched with saturated aqueous NH_4Cl, extracted with ether, and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the crude product was submitted to a flash chromatographic purification (hexane/ethyl acetate (7:3)) affording 0.815 g (88%) of **3l** as an inseparable mixture of diastereomers: oil, IR (cm^{-1}, neat) 3480 (OH), 3045 (=CH), 1525 (NO_2); trans isomer: ^{1}H-NMR δ 1.25–1.40 (3H, m), 1.60–2.20 (5H, m), 2.48 (2H, d, J = 9.2), 2.96 (1H, s, OH), 4.44 (1H, dd, J = 11.7, 4.4, $CHNO_2$), 5.10–5.22 (2H, m), 5.78–5.85 (1H, m); MS m/z 154, 139, 128, 115, 76, 63, 51; cis isomer ^{1}H-NMR δ 1.25–1.40 (3H, m), 1.60–2.20 (5H, m), 2.42 (2H, d, J = 8.2), 4.47 (1H, dd, J = 11.9, 4.4, $CHNO_2$), 5.10–5.22 (2H, m), 5.30 (1H, s, OH), 5.80–5.89 (1H, m); MS m/z 154, 144, 98, 80, 69, 55, 41. Anal. Calcd for $C_9H_{15}NO_3$ (185.22): C, 58.36; H, 8.16; N, 7.56. Found: C, 58.38; H, 8.20; N, 7.52.

Reaction between α-Nitrocyclopentanone (6) and Grignard and Lithium Reagents. 1-Methyl-2-nitrocyclopentene (7). The same experimental procedure as above was followed: oil; IR (cm^{-1}, neat) 1635 (C=C), 1495 (NO_2); ^{1}H-NMR δ 1.90–2.03 (2H, m), 2.20 (3H, s), 2.60–2.70 (2H, m), 2.85–3.00 (2H, m); MS m/z 127 (M^+), 110, 98, 79, 55, 53, 41, 39. Anal. Calcd for $C_6H_9NO_2$ (127.4): C, 56.68; H, 7.13; N, 11.01. Found: C, 56.67; H, 7.13; N, 11.00.

1-Propyl-2-nitrocyclopentene (8): yield 78%; oil; IR (cm^{-1}, neat) 1630 (C=C), 1540 (NO_2); ^{1}H-NMR δ 0.97 (3H, t, 7.4), 1.45–1.60 (2H, m), 1.85–2.00 (2H, m), 2.58–2.65 (4H, m), 2.90–3.00 (2H, m); MS m/z 155 (M^+), 154, 130, 102, 96, 83, 55, 41, 39. Anal. Calcd for $C_8H_{13}NO_2$ (155.20): C, 61.91; H, 8.44; N, 9.02. Found: C, 61.87; H, 8.43; N, 8.99.

Reaction between 2-Nitro-3-pentanone (10) and Lithium Reagents. 3-Methyl-2-nitro-3-pentanol (11a). The same experimental procedure as above was followed: yield 78%; oil; IR (cm^{-1}, neat) 3450 (OH), 1520 (NO_2); syn isomer ^{1}H-NMR δ 1.00 (3H, t, J = 7.0), 1.20 (3H, s), 1.40–1.60 (5H, m), 3.65 (1H, s, OH), 4.55 (1H, q, J = 6.8, $CHNO_2$); anti isomer 0.95 (3H, t, J = 7.0), 1.15 (3H, s), 1.40–1.62 (5H, m), 2.70 (1H, s, OH), 4.60 (1H, q, J = 6.8, $CHNO_2$); MS m/z 132, 118, 76, 73, 58, 43. Anal. Calcd for $C_6H_{13}NO_3$ (147.17): C, 48.96; H, 8.90; N, 9.52. Found: C, 48.95; H, 8.87; 9.52.

3-Ethyl-2-nitro-3-heptanol (11b): yield 92%; oil; IR (cm^{-1}, neat) 3530 (OH), 1545 (NO_2); ^{1}H-NMR δ 0.85–0.95 (6H, m), 1.20–1.70 (11H, m), 3.60 (1H, s, OH), 4.65 (1H, q, J = 6.8, $CHNO_2$); MS m/z 161, 149, 115, 103, 85, 57, 43. Anal. Calcd for $C_9H_{19}NO_3$ (189.26): C, 57.12; H, 10.12; N, 7.40. Found: C, 57.10; H, 10.15; N, 7.44.

2-Nitro-3-phenyl-3-pentanol (11c): yield 85%; oil; IR (cm^{-1}, neat) 3565 (OH), 1530 (NO_2); ^{1}H-NMR δ 0.85 (3H, t, J = 7.0), 1.75 (3H, d, J = 6.9), 1.85–2.00 (2H, m), 3.70 (1H, s, OH), 5.05 (1H, q, J = 6.9, $CHNO_2$), 7.20–7.25 (5H, m); MS m/z 170, 169, 135, 105, 77, 65, 57, 43. Anal. Calcd for $C_{11}H_{15}NO_3$ (209.25): C, 63.14; H, 7.22; N, 6.69. Found: C, 63.13; H, 7.25; N, 6.70.

3-(1,3-Dithian-2-yl)-2-nitro-3-pentanol (11d): yield 87%; mp 117 °C (from hexane); IR (cm^{-1}, KBr) 3400 (OH), 1535 (NO_2); ^{1}H-NMR δ 1.10 (3H, t, J = 7.0), 1.70 (3H, d, J = 6.9), 2.00–2.15 (2H, m), 2.60–2.80 (3H, m), 2.95–3.15 (3H, m), 3.20 (1H, s, OH), 4.30 (1H, s), 5.25 (1H, q, J = 6.9, $CHNO_2$); MS m/z 217, 176, 149, 119, 57, 45, 43. Anal. Calcd for $C_9H_{15}NO_3S_2$ (249.34): C, 43.35; H, 6.06; N, 5.61. Found: C, 43.23; H, 7.25; N, 5.55.

3-Ethyl-4-nitro-1-phenyl-1-pentyn-3-ol (11e): yield 90%; oil; IR (cm^{-1}, neat) 3400 (OH), 2200 (C–C triple bond), 1530 (NO_2); ^{1}H-NMR δ 1.15 (3H, t, J = 7.0), 1.70 (3H, d, J = 6.8), 1.90–2.00 (2H, m), 3.20 (1H, s, OH), 4.80 (1H, q, J = 6.8, $CHNO_2$), 7.25–7.35 (5H, m); MS m/z 158, 129, 101, 77, 75, 65, 57, 51, 43. Anal. Calcd for $C_{13}H_{15}NO_3$ (233.27): C, 66.93; H, 6.48; N, 6.00. Found: C, 66.94; H, 6.45; N, 5.98.

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