# Regio-, Stereo-, and Enantioselectivity in the Electrophilic Reactions of 2-Amino-4-phenyl-3-butenenitriles

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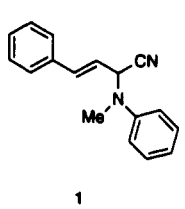
*Received August 27, 1992*

The allylic anion generated from 2-(*N*-methylanilino)-4-phenyl-3-butenenitrile (1) reacted with iodomethane and 3-bromo-1-chloropropane in THF/HMPA to give the γ-substitution products exclusively, predominantly in the 2*Z*-configuration. Substitution of the *N*-methylanilino group with the methyl ether of L-(−)-ephedrine resulted in the generation of chiral aminonitrile 2. Lithiated 2 reacted sluggishly in THF with allyl bromide and benzyl chloride in the absence of HMPA to give the γ-substitution products predominantly in the 2*Z*-configuration, with little diastereoselectivity. The aminonitrile 3 prepared from cinnamaldehyde, L-(−)-ephedrine, and KCN was lithiated with 2 equiv of LDA resulting in high facial selectivity (76–100% diastereomeric excess) in alkylations in the presence of HMPA and LiI. Lithiated 3 reacted with propionaldehyde, benzaldehyde, and *p*-bromobenzaldehyde at −78 °C to give the γ-addition products, predominantly in the 4*R*-configuration (64–78% de). The stereochemistry of the isomers of each product was determined by chemical correlation and spectral methods including analyses of the CD spectra and X-ray diffraction. A bicyclic transition state C wherein lithium is chelated by both amino and alkoxy groups is proposed to interpret the observed stereoselectivity.

## Introduction

α-Aminonitrile anions have been used extensively as nucleophilic acyl equivalents.[1] The allylic anion generated from a vinyl or alkylidenyl α-aminonitrile can function as an equivalent for the β-anion of a carboxylic acid when reaction occurs at the γ-site.[2] Such behavior was observed in the cinnamyl anion generated from 2-(*N*-methylanilino)-4-phenylbutenenitrile (1) which undergoes γ-substitution exclusively with haloalkanes.[2a] In this case, α-alkylation was presumably disfavored by the presence of the bulky *N*-methylanilino group.[3] Following our preliminary studies[4] which demonstrated that alkylations in the presence of a dipolar medium (HMPA) give γ-substituted products predominantly in the 2*Z* configuration, we went on to investigate the electrophilic reactions of the allyl anions generated from 2 and 3, which contain chiral auxiliaries derived from L-(−)-ephedrine or *O*-methyl-L-(−)-ephedrine.

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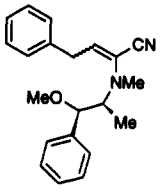


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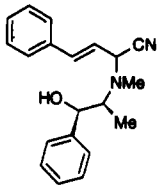


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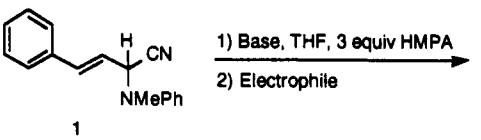
## Results and Discussion

**Alkylation Reactions of 1.** The aminonitrile 1 was prepared by condensation of equimolar amounts of cinnamaldehyde, potassium cyanide, and *N*-methylaniline.[2a,5] The cinnamyl anion of 1 was readily generated by treatment of 1 with LDA in THF at −78 °C; its reactions with iodomethane and 2-bromopropane, however, were sluggish.[2a] The alkylating reactions were accelerated by the addition of HMPA. Methylation occurred at −78 °C in the presence of HMPA to give the γ-product 5 exclusively in the *Z*-configuration. When the alkylating reactions were performed at room temperature (Table I), the products contained some *E*-isomers (entries 4 and 6). Protonation of the lithiated 1 resulted in a similar bias in the stereochemistry in favor of the *Z*-isomer. However, alkylation of 1 with *o*-bromobenzyl bromide at

**Table I. Protonation and Alkylations of the Allylic Anion of the Aminonitrile 1**

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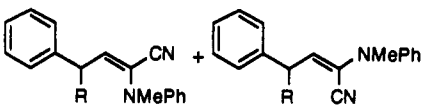


Z-γ-product E-γ-product

4 R = H 6 R = $Cl(CH_2)_3$
5 Me 7 o-$BrC_6H_4CH_2$

| entry | electrophile | base | reaction condns, *T*, °C (time, h) | products (total yield, %), *Z*:*E* |
|---|---|---|---|---|
| 1 | MeOH | LDA | −78 (0.5) | 4 (90), 100:0 |
| 2 | $NH_4Cl$ | LDA | −78 to rt (1) | 4 (92), 74:26 |
| 3 | MeI | LDA | −78 (1) | 5 (81), 100:0 |
| 4 | MeI | LDA | −78 to rt (1) | 5 (84), 79:21 |
| 5 | $Br(CH_2)_3Cl$ | LDA | −78 (1) | 6 (86), 100:0 |
| 6 | $Br(CH_2)_3Cl$ | LDA | −78 to rt (1) | 6 (86), 68:32 |
| 7 | o-$BrC_6H_4CH_2Br$ | *t*-BuOK | 0 to rt (1) | 7 (87), 17:83 |

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(1) For reviews: (a) Albright, J. D. *Tetrahedron* **1983**, *39*, 3207. (b) Hase, T. A. Ed., *Umpoled Synthons*, Wiley: New York, 1987.

(2) (a) Ahlbrecht, H.; Vonderheid, C. *Synthesis* **1975**, 512. (b) Ahlbrecht, H.; Liesching, D. *Synthesis* **1977**, 495. (c) Fang, J.-M.; Liao, L.-F.; Yang, C.-C. *Proc. Natl. Sci. Council (Taipei)*, **1985**, *9*, 1.

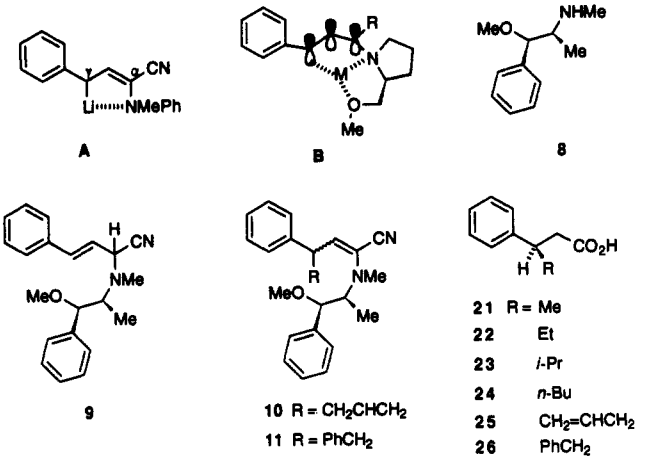
(3) See ref. 2a: The analog of 1 having a piperidino or a dimethylamino group instead of the *N*-methylanilino group undergoes alkylation at both the α- and γ-sites.

(4) (a) Fang, J.-M.; Chang, H. T.; Lin, C.-C. *J. Chem. Soc., Chem. Commun.* **1988**, 1385. (b) Fang, J.-M.; Chang, C.-J. *J. Chem. Soc., Chem. Commun.* **1989**, 1787.

(5) Strecker, A. *Ann.* **1850**, *27*, 75.

0022-3263/93/1958-1754$04.00/0 

room temperature using *t*-BuOK as base gave **7**, predominantly in the *E*-configuration. The configurations of **4–7** were readily determined from their NMR spectra,[6] in which the resonances due to H-3 in the *Z*-isomers appeared at lower fields (δ 6.28–6.65) than those of the corresponding *E*-isomers (δ 5.63–5.97). The C-3 resonance of the *Z*-isomer (around δ 145) was also diagnostic. The nature of the allylic anions with heteroatoms or cyano substituents was unclear,[7] although the working hypothesis that assumes an intermediate **A** could account for the observed regio- and stereoselectivity when LDA was used as the base. The bulky *N*-methylanilino group in **A** would discourage α-alkylations while its coordination with lithium[8] might induce the formation of the *Z*-products.




**Asymmetric Alkylation Reactions of 2.** Ahlbrecht et al.[11] have reported the asymmetric alkylations of the metalated allylamines (or enamines) **B** using L-proline methyl ether as the chiral auxiliary. From the evidence of the X-ray analysis and MNDO calculations,[12] the nucleophilic species was judged to be a delocalized 3-metalated enamine structure in which lithium is chelated to both the amino and alkoxy groups. Our initial work involved the use of L-(−)-ephedrine methyl ether (**8**)[10] as a chiral surrogate for the *N*-methylanilino group in **1** to study the alkylation of the anion of **2**. Accordingly, condensation of the perchlorate salt of **8** with cinnamaldehyde and KCN (1 equiv)[5] afforded the styryl amino nitrile **9**, which decomposed during attempted chromatography on silica gel. When an excess of KCN was used, the primarily formed **9** isomerized in situ to give the conjugated aminonitrile **2** as a mixture of *E*/*Z* isomers (5:7). An experiment in which the *E*/*Z* mixture (2:9) was treated with LDA in THF at room temperature and then protonated with aqueous $NH_4Cl$ gave **2** as a single *E*-isomer. The lithiated **2** was inert to alkylating agents at −78 °C, but reacted with allyl bromide at room temperature to give 50% of the γ-substitution product **10** as a mixture of four diastereomers, predominantly in the *Z*-configuration. The allylation showed no diastereoselectivity at the newly formed C-4 stereocenter. The alkylation with benzyl chloride at room temperature afforded two *E*-γ-products **11**, predominantly in the 4*R*-configuration 24% diastereomeric excess (de). The stereochemistries of **10** and **11** were determined following their transformations into the corresponding β-substituted carboxylic acids **24** and **25**, similar to the method used for **17** and **18** (see below). At this point, we did not test other parameters such as solvent and countercation, which might increase the de, but instead investigated the use of the more readily available L-(−)-ephedrine as an auxiliary.[13]

**Asymmetric Alkylating Reactions of 3.** The chiral substrate was similarly prepared from L-(−)-ephedrine hydrochloride according to Strecker's method.[5] The yellow crystalline compound **3** consisted of equal amounts of C-2 epimers; separation of these two epimers was unnecessary, however, as the H-2 was to be removed in subsequent reactions. Transformation of **3** into a single isomer of conjugated alkenenitrile **12a** (*Z*-configuration) was achieved by removal of H-2 with the strong base LDA (2 equiv), followed by protonation at C-4 with aqueous $NH_4Cl$ at −78 °C. On the other hand, treatment of **3** with LDA at 0 °C for 20 min afforded the *E*-isomer (**12b**) exclusively. Isomerization of **3** to **12** was also carried out using other bases such as *t*-BuOK, DABCO, and DBU (but not $Et_3N$). The isomerization experiments indicated that the *Z*-isomer is a kinetic product but that the *E*-isomer is thermodynamically favored. The lithiated **3** did not react with MeI at −78 °C in THF; however, a 55% yield of the methylated products **13** was obtained when the mixture was warmed to room temperature. The methylation was greatly facilitated by the assistance of HMPA (3 equiv) to give 69% of **13** at −78 °C. No formation of O-alkylated compounds[9] was observed.

The reactions of **3** with other haloalkanes and diphenyl disulfide were performed under various conditions, and the results are listed in Table II (N*H representing L-ephedrine). Each reaction should, in principle, yield four γ-substitution products, designated **a**, **b**, **c**, and **d** series, having respectively the (2*Z*,4*R*)-, (2*E*,4*R*)-, (2*Z*,4*S*)-, and (2*E*,4*S*)-configurations. Reactions at −78 °C seemed to give higher de than those conducted at −100 °C or at room temperature (compare entries 3–5). The reaction in the presence of LiI (1 equiv) and HMPA (3 equiv) at −78 °C proceeded rapidly to give the highest ratio of γ-substitution products having the (2*Z*,4*R*)-configuration. However, both yield and stereoselectivity decreased if LiI was used alone, without HMPA (compare entries 17–19). The combination of allyl bromide and LiI, in the presence of HMPA, gave better stereoselectivity than the reaction with allyl iodide (compare entires 12 and 15). In contrast,

(6) (a) Costisella, B.; Gross, H. *Tetrahedron* **1982**, *38*, 139. (b) Fang, J.-M.; Yang, C.-C.; Wang, Y.-W. *J. Org. Chem.* **1989**, *54*, 477.

(7) (a) Schlosser, M.; Stahle, M. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 487. (b) Biellmann, J. F.; Ducep, J. B. *Org. React.* **1982**, *27*, 1. (c) Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React.* **1984**, *31*, 1.

(8) Some representative examples: (a) Meyers, A. I. *Acc. Chem. Res.* **1978**, *11*, 375. (b) Fitt, J.-J.; Gschwend, H.-W. *J. Org. Chem.* **1979**, *44*, 303. (c) Narasaka, K.; Miwa, T.; Hayashi, H.; Ohta, M. *Chem. Lett.* **1984**, 1399. (d) Lamothe, S.; Chan, T.-H. *Tetrahedron Lett.* **1991**, *32*, 1847. (e) Sielecki, T. M.; Meyers, A. I. *J. Org. Chem.* **1992**, *57*, 3673 and references cited therein.

(9) (a) Meyers, A. I.; Poindexter, G. S.; Brich, Z. *J. Org. Chem.* **1978**, *43*, 892. (b) Naslund, J; Welch, C. J. *Tetrahedron Asym.* **1991**, *2*, 1123.

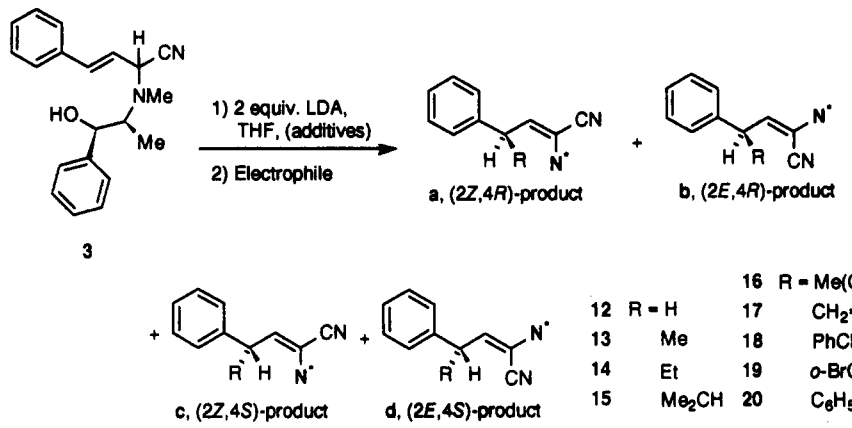
(10) Enders, D.; Fey, P.; Kipphardt, H. *Org. Synthesis* **1987**, *65*, 173.

(11) (a) Ahlbrecht, H; Bonnet, G.; Enders, D.; Zimmermann, G. *Tetrahedron Lett.* **1980**, *21*, 3175. (b) Enders, D. in *Current Trends in Organic Synthesis*, Nozaki, H. Ed., **1982**. (c) Ahlbrecht, H.; Sommer, H. *Chem. Ber.* **1990**, *123*, 829.

(12) Ahlbrecht, H.; Bocle, G.; Harms, K.; Marsch, M.; Sommer, H. *Chem. Ber.* **1990**, 1853.

(13) For general reviews: (a) Valentine, Jr., D.; Scott, J. W. *Synthesis* **1978**, 329. (b) Tomioka, K. *Synthesis* **1990**, 541. Some representative examples: (c) Larcheveque, M.; Ignatove, E.; Cuvigny, T. *Tetrahedron Lett.* **1978**, 3961. (d) Mukaiyama, T.; Iwasawa, N. *Chem. Lett.* **1981**, 913. (e) Joshi, N. N.; Srebnik, M.; Brown, H. C. *Tetrahedron Lett.* **1989**, *30*, 5551. (f) Alexakis, A.; Mutti, S.; Normant, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 6332. (g) Heaton, S. B.; Jones, G. B. *Tetrahedron Lett.* **1992**, *33*, 1693.

**Table II. Reactions of the Anion of 3 with Haloalkanes and Diphenyl Disulfide**




| entry | halide | additives (equiv) | reactn condns, $T$, °C (time) | products[a] (total yield, %), a:b:c:d | diaster. excess,[b] % |
|---|---|---|---|---|---|
| 1 | MeI | | −78 to rt over 3 h | 13 (55), 38:40:2:20 | 56 |
| 2 | MeI | HMPA (3) | −78 (25 min) | 13 (69), 65:23:0:12 | 76 |
| 3 | EtI | | −78 to rt over 3 h | 14 (28), 0:50:0:50 | 0 |
| 4 | EtI | HMPA (3) | −78 (50 min) | 14 (70), 52:36:0:12 | 76 |
| 5 | EtI | HMPA (3) | −110 (25 min) | 14 (73), 40:43:0:17 | 66 |
| 6 | EtI | HMPA (3), LiI (1) | −78 (25 min) | 14 (68), 65:27:0:8 | 84 |
| 7 | *i*-PrI | HMPA (3) | −78 (30 min) | 15 (52), 56:22:0:22 | 56 |
| 8 | *n*-BuI | HMPA (3) | −78 (1 h) | 16 (71), 62:25:0:13 | 74 |
| 9 | *n*-BuI | HMPA (3), LiI (1) | −78 (45 min) | 16 (84), 61:27:0:12 | 76 |
| 10 | $CH_2$=$CHCH_2Br$ | | −78 to rt over 3 h | 17 (55), 42:36:0:22 | 56 |
| 11 | $CH_2$=$CHCH_2Br$ | HMPA (3) | −78 (15 min) | 17 (73), 49:29:7:15 | 56 |
| 12 | $CH_2$=$CHCH_2Br$ | HMPA (3), LiI (1) | −78 (10 min) | 17 (69), 74:18:0:8 | 84 |
| 13 | $CH_2$=$CHCH_2Br$ | HMPA (3), LiI (1) | −110 (10 min) | 17 (62), 50:40:0:10 | 80 |
| 14 | $CH_2$=$CHCH_2Br$ | $MgCl_2$ (1) | −78 (2 h) | 17 (15), 0:50:0:50[c] | 0 |
| 15 | $CH_2$=$CHCH_2I$ | HMPA (3) | −78 (10 min) | 17 (87), 52:27:8:13 | 58 |
| 16 | $PhCH_2Br$ | | −78 to rt over 3 h | 18 (77), 56:22:0:22 | 56 |
| 17 | $PhCH_2Br$ | HMPA (3) | −78 (25 min) | 18 (76), 80:11:0:9 | 82 |
| 18 | $PhCH_2Br$ | LiI (1) | −78 (20 min) | 18 (32), 32:0:0:0 | 32 |
| 19 | $PhCH_2Br$ | HMPA (3), LiI (1) | −78 (10 min) | 18 (78), 85:15:0:0 | 100 |
| 20 | *o*-$BrC_6H_4CH_2Br$ | | −78 to rt over 1 h | 19 (63), 42:37:3:18 | 58 |
| 21 | *o*-$BrC_6H_4CH_2Br$ | HMPA (3) | −78 (1 h) | 19 (73), 70:19:0:22 | 78 |
| 22 | *o*-$BrC_6H_4CH_2Br$ | LiI (1) | −78 (2 h) | 19 (53), 40:38:0:22 | 56 |
| 23 | *o*-$BrC_6H_4CH_2Br$ | HMPA (3), LiI (1) | −78 (1 h) | 19 (75), 72:17:0:11 | 78 |
| 24 | PhSSPh | HMPA (3) | −78 (15 min) | 20 (60), 44:14:28:14 | 16 |
| 25 | PhSSPh | HMPA (3), LiI (1) | −78 (10 min) | 20 (43), 70:15:0:15 | 70 |

[a] Series a, b, c, and d represent compounds having configurations (2*Z*,4*R*), (2*E*,4*R*), (2*Z*,4*S*), and (2*E*,4*S*), respectively. [b] The diastereomeric excess indicates the difference between 4*R*- and 4*S*-products, the value was calculated from (a + b) − (c + d). [c] Compound **12** (R = H) having the *Z*-configuration was recovered in 45% yield.

allylation in the presence of $MgCl_2$ gave a low yield of **17** and no stereoselectivity at the C-4 center. Poor selectivity was also found in the allylation of **3** with (diisopropylamino)magnesium chloride as the base.

The isomers of γ-substitution products **13–20** were separated by chromatography and their structures determined by their spectral data (IR, MS, and $^1H$ and $^{13}C$ NMR) along with an x-ray analysis of the benzylated compound **18a**. Subsequently hydrolysis[2a] of the individual products with oxalic acid in refluxing aqueous THF gave rise to the corresponding carboxylic acids **21–26**, whose chirality was assigned by comparison of the optical rotations with the known values.[14] For example, **18a** was hydrolyzed to give the (*R*)-acid **26**, $[\alpha]^{25}_D$ +52° (lit.[14] $[\alpha]^{25}_D$ +59° in benzene). The stereostructures of the isomers in **17**, **19**, and **20** were assigned by analyses of their NMR spectra, with special attention being paid to the differences in chemical shifts of H-3, 1′ and 2′.

**Reactions of 3 with Aldehydes, 2-Cyclohexenone, and Methyl Crotonate.** The chiral lithiated **3** reacted with propionaldehyde at −78 °C to give **27a–c** (67:22:11) out of eight possible isomers (Table III). Compounds **27a–c** (*Z*-configuration) displayed the H-3 resonances at δ 6.37, 6.53, and 6.43, respectively.[6] The relative erythro-configuration of **27a** and **27c** was demonstrated by hydrolysis to the cis lactones **30a** and **30c** (a pair of enantiomers),[2a] respectively. Hydrolysis of the threo isomer **27b** afforded the trans lactone **30b**. The H-4 and H-5 resonances in **30a** (or **30c**) occurred at δ 3.72 and 4.61, while the corresponding resonances in **30b** appeared at higher fields (δ 3.27 and 4.37) due to the shielding effect of the adjacent ethyl or phenyl group.[15] Sequential transformation of **27a**, via reduction of the corresponding lactone **30a**,[19] yielded (*R*)-3-phenylhexanol (lit.[16] $[\alpha]^{25}_D$ −6.5°). Overreduction of **27b** and **27c** gave rise to (*S*)-3-phenylhexane and its enantiomer,[16] respectively. Thus,

(14) (a) Rupe, H. *Ann.* **1909**, *369*, 311. (b) Kawana, K.; Emoto, S.; *Bull. Chem. Soc. Jpn.*, **1966**, *39*, 910. (c) Mukaiyama, T.; Takeda, T.; Fujimoto, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3368. (d) Meyers, A. I.; Smith, R. K.; Whitten, C. E. *J. Org. Chem.* **1979**, *44*, 2250. (e) Soai, K.; Ookawa, A. *J. Chem. Soc., Perkin Trans. 1*, **1986**, 759. (f) Tomioka, K.; Suenaga, T.; Koga, K. *Tetrahedron Lett.* **1985**, *26*, 6051.

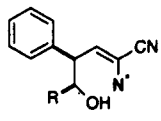
(15) (a) Hoppe, D.; Bronneke, A. *Tetrahedron Lett.* **1983**, *24*, 1687. (b) Fang, J.-M.; Liao, L.-F.; Hong, B.-C. *J. Org. Chem.* **1986**, *51*, 2828. (c) Fang, J.-M.; Chen, M.-Y.; Yang, W.-J. *Tetrahedron Lett.* **1988**, *29*, 5937.

(16) (a) Levene, P. A.; Markov, R. E. *J. Biol. Chem.* **1932**, *93*, 749. (b) Borsook, H.; Huffman, H. M.; Liu, Y. P. *J. Biol. Chem.* **1941**, *102*, 449.

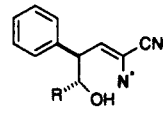
**Table III. Addition Reactions of the Anion of 3 with Aldehydes, 2-Cyclohexenone, and Methyl Crotonate**

| entry | electrophile | reactn condns, *T*, °C (time, h) | products (total yield, %), isomeric ratio[a] | diaster excess at C-4 |
|---|---|---|---|---|
| 1 | EtCHO | −78 (1) | **27** (58), **a**:**b**:**c** = 67:22:11 | 78 (*R*) |
| 2 | EtCHO | HMPA (3 equiv), −78 (1) | **27** (52), **a**:**b**:**c**:**d**:**f** = 25:4:13:15:43 | 44 (*R*) |
| 3 | $C_6H_5CHO$ | −78 (1) | **28** (67), **a**:**b**:**d** = 60:25:15 | 70 (*R*) |
| 4 | *p*-$BrC_6H_4CHO$ | −78 (1) | **29** (76), **a**:**b**:**d**:**f** = 32:45:18:5 | 64 (*R*) |
| 5 | 2-cyclohexenone | −78 (1.5) and warmed to −30 over 3 h | **33**[b] (66), 36:36:18:10 | |
| 6 | methyl crotonate | −78 (1) and warmed to −30 over 2 h | **34**[b] (73), 40:20:27:13 | |
| 7 | methyl crotonate | HMPA (2 equiv), −78 (1) | **34**[b] (82), 67:33 | |

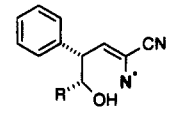
[a] Series **a**, **b**, **c**, **d**, and **f** represent compounds having configurations (2*Z*,4*R*-erythro), (2*Z*,4*R*-threo), (2*Z*,4*S*-erythro), (2*Z*,4*S*-threo), and (2*E*,4*R*-threo), respectively. No isomers **e**, **g**, or **h** having the configuration (2*E*,4*R*-erythro), (2*E*,4*S*-erythro), or (2*E*,4*S*-threo) were isolated. [b] The configurations of the products were not determined.



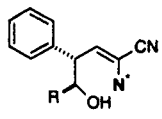
(2*Z*, 4*R*)-erythro
**27a** R = Et
**28a** R = Ph
**29a** R = *o*-$BrC_6H_4$



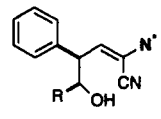
(2*Z*, 4*R*)-threo
**27b-29b**



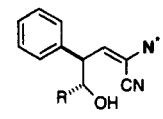
(2*Z*, 4*S*)-erythro
**27c-29c**



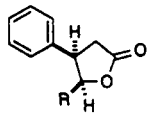
(2*Z*, 4*S*)-threo
**27d-29d**



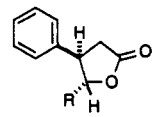
(2*E*, 4*R*)-erythro
**27e-29e**



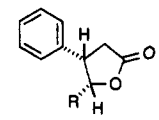
(2*E*, 4*R*)-threo
**27f-29f**



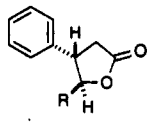
(4*R*)-cis
**30a** R = Et
**31a** R = Ph
**32a** R = *o*-$BrC_6H_4$



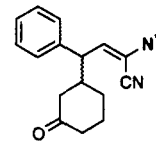
(4*R*)-trans
**30b-32b**



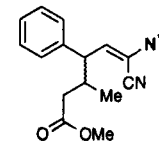
(4*S*)-cis
**30c-32c**



(4*S*)-trans
**30d-32d**



**33**



**34**

**27a–c** with (2*Z*,4*R*,5*S*)-, (2*Z*,4*R*,5*R*)-, and (2*Z*,4*S*,5*R*)-configurations, respectively, indicated the preference for the 4*R*-chirality (78% de) and the relative erythro configuration. The lithiated **3** reacted with propionaldehyde in the presence of HMPA to afford 5 isomers **27a–d** and **27f** (25:4:13:15:43). The major product **27f** was shown to have the (2*E*,4*R*,5*R*)-configuration by analysis of its $^1H$ NMR spectrum as well as by hydrolysis to give the trans lactone **30b**. The structure of **27d** was similarly determined to be the (2*Z*,4*S*,5*S*)-configuration, which led to an enantiomer of **30b** after hydrolysis. The presence of HMPA enhanced the formation of the thermodynamically favored isomers having *E*- and threo-configurations, suggesting an intrinsic reversibility for the addition reaction of aldehydes. The addition reactions of **3** with benzaldehyde and *p*-bromobenzaldehyde were performed in the absence of HMPA to afford, respectively, **28** and **29** with predominantly 4*R*-chirality (70% and 64% de, respectively). The stereostructures of **28** and **29** were similarly determined by transformation of the individual isomers into the corresponding lactones **31** and **32**, along with analysis of their CD spectra. For example, the adduct **29b** with (2*Z*,4*R*,5*S*)-configuration was hydrolyzed with aqueous oxalic acid to give trans lactone **32b** with (4*R*,5*S*)-configuration. The coupling constant of 8.8 Hz for $J_{4,5}$ in **32b** is attributed to a 165° dihedral angle between H-4 and H-5. A molecular model indicates that the bonds of $C_4$-Ph and $C_5$-Ar are nearly perpendicular.[17] Thus, the positive Cotton effect with maximum amplitude appearing at 224 nm in the CD spectrum of **32b** was consistent with the assigned (4*R*,5*S*)-configuration, according to the exciton coupling theory.[18] Since both **32a** and **32b** were converted to an (*S*)-1-(4-bromophenyl)-2-phenylbutane, the cis lactone **32a** should have the (4*R*)-configuration and its precursor **29a** had the (4*R*,5*R*)-configuration. The structure of **29d** was deduced by its conversion to the lactone **32d**, a mirror image of **32b**. Hydrolysis of **29f** yielded a trans lactone **32b**, thus confirming its (4*R*,5*S*)-configuration.

The lithiated **3** underwent Michael addition with 2-cyclohexenone in THF to give **33** as a mixture of four isomers, predominantly in the *E*-configuration. The reaction with methyl crotonate gave four *E*-isomers of the conjugate adduct **34** (40:20:27:13). Only the two former isomers were obtained when the reaction was conducted in the presence of HMPA (entry 6, Table III). Enders et al.[19] have recently reported the enantioselective Michael addition of a lithiated chiral amino cyanide to several α,β-unsaturated esters. Although the stereostructures of the Michael adducts **33** and **34** might be deduced by analogy to related reaction mechanisms, their stereostructures were not rigorously determined.

**Reaction Mechanism.** By substitution of *N*-methylaniline with L-(−)-ephedrine, a bicyclic transition state **C** in which lithium is chelated by both amino and alkoxy groups may facilitate the approach of electrophiles to the exo-face to give products with the observed (2*Z*,4*R*)-configuration. This model is similar to that of aminoallyllithium **B** (R = Ph). Although **C** is assumed to have a planar ($sp^2$ hybridized) C-4 center, its counterpart **C′** with a pyramidal ($sp^3$ hybridized) C-4 center would also lead to the same facial selectivity.[20] It was noted that the crystal structure of **18a**, with the hydroxyl group and lone pair of the nitrogen atom oriented to the endo-face, closely

(17) A crystal structure of the trans lactone **32b**/**32d** racemate indicated that the dihedral angle of $C_4$-Ph/$C_5$-Ar was 81°.

(18) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy – Exciton Coupling in Organic Stereochemistry*; University Science Books: 1983.

(19) Enders, D.; Gerdes, P.; Kipphandt, H. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 179.

(20) For discussion of $sp^2$- or $sp^3$-hybridized carbanions, see: Castonguay, L. A.; Cuiles, J. W.; Rappe, A. K.; Meyers, A. I. *J. Org. Chem.* **1992**, *57*, 3819 and the references cited therein.

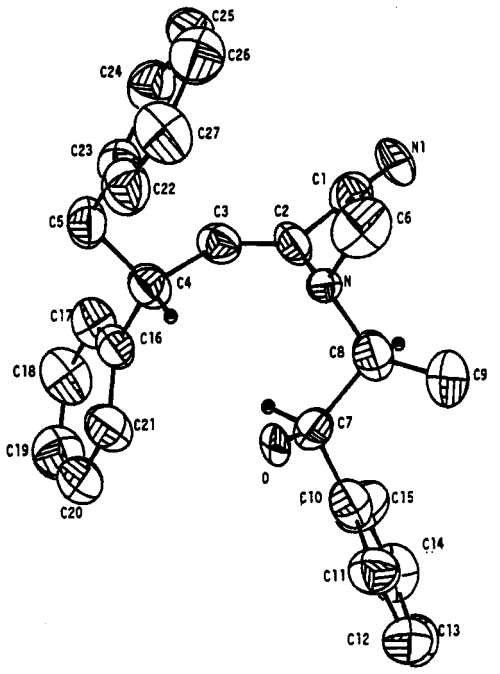
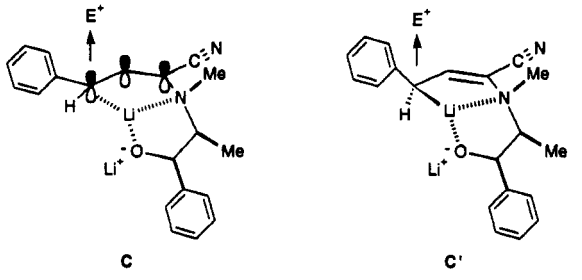



**Figure 1.** ORTEP drawing of 18a.

resembles the proposed structure C (or C'). On the basis of the experimental data, the reactivity and stereoselectivity shown in Tables II and III might reflect aggregation states of the reacting species.[21] High reactivity at −78 °C seems to be essential to inducing the diastereoselectivity at the newly formed C-4 center. A dipolar co-solvent (HMPA) was needed in order to accelerate the reactions with less reactive electrophiles and thus give enhanced diastereoselectivity, but HMPA decreased selectivity in the reactions with aldehydes. Addition of LiI tended to lessen the degree of aggregation[19] and thereby increased stereoselectivity in the alkylations. The opposite effect was obtained in the presence of divalent magnesium ion, which is believed to cause tight aggregation through its powerful coordinating ability.[22]




C C'

## Experimental Section

General information concerning instrumentation and materials was described previously.[23] Iodoalkanes were distilled and stored in the presence of a piece of copper wire before use. L-(−)-Ephedrine hydrochloride was commercially available reagent grade, mp 210–212 °C, $[\alpha]^{25}_D$ −31.9° (*c* 6.7, $H_2O$). The ratio of products was determined by HPLC and $^1H$ NMR analyses and was occasionally assisted by the measurement of isolated weights of the products. 2-(*N*-Methyl-*N*-phenylamino)-3-butenenitrile (1) and its methylated product 2-(*N*-methylanilino)-4-phenyl-2-pentenenitrile (5) were prepared according to the procedure described in ref. 2a.

**Preparation of 2-[*N*-Methyl-*N*-(2-methoxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-butenenitrile (2) and 2-[*N*-Methyl-*N*-(2-methoxy-1-methyl-2-phenylethyl)amino]-4-phenyl-3-butenenitrile (9) via (1*R*,2*S*)-α-[1-(Methylamino)ethyl]benzyl Methyl Ether (8).** L-(−)-Ephedrine (1.98 g, 12 mmol) was treated with methyl formate (4.8 mL) at room temperature for 5 h, and the reaction mixture was concentrated in vacuo to give a quantitative yield (2.32 g) of the corresponding formamide containing two tautomers. The formamide was dissolved in THF (10 mL) and cooled to −60 °C, and MeI (0.93 mL, 15 mmol) was added dropwise followed by NaH (0.32 g, 15 mmol, prewashed with hexane). The cooling bath was removed, and the mixture was stirred at room temperature for 30 min and heated under reflux for 2 h. The mixture was cooled, the solvent was removed, and the residue was chromatographed on silica gel (EtOAc/hexane (60:40)) to give the formamide of the ephedrine methyl ether 8 (2.31 g, 93%), which contained two tautomers.

The product was dissolved in THF (10 mL) and treated with MeMgCl (13.3 mmol, 4.9 mL of a 2.7 M solution in THF) at 0 °C under $N_2$. The mixture was stirred at room temperature for 2 h and poured slowly into ice-cooled brine. After addition of saturated aqueous $NH_4Cl$ (1 mL), the mixture was extracted with EtOAc. The organic phase was dried ($Na_2SO_4$) and concentrated. The residue was chromatographed on silica gel ($Et_3N$/EtOAc (1:99)) to give the methyl ether 8 (1.88 g, 95%), which was dissolved in $Et_2O$ and treated with 1 equiv of $HClO_4$ (70% aqueous solution) to give 2.79 g (95%) of the perchlorate salt, $[\alpha]^{25}_D$ = −66.6° (*c* 10, $CHCl_3$).

The perchlorate salt was dissolved in $CH_3CN$ (5 mL), and cinnamaldehyde (1.32 g, 10 mmol), aqueous KCN (20 mmol, 1.3 g in 2 mL of water), $Et_2O$ (3 mL), and benzyltriethylammonium chloride (small amount) were added. The orange mixture was stirred at room temperature for 5 h and extracted with EtOAc. The combined extracts were dried ($Na_2SO_4$) and concentrated in vacuo. The residue was chromatographed on silica gel (EtOAc/hexane (5:95)) to give the *E*-isomer (1.62 g, $R_f$ 0.30) and the *Z*-isomer (1.16 g, $R_f$ 0.27) of the conjugated aminonitrile 2[9] in 87% total yield. *E*-Isomer: an oil; $^{13}C$ NMR ($CDCl_3$) δ 12.5 (q, C-3'), 32.1 (q, $NCH_3$), 35.7 (t, C-4), 56.7 (q, $OCH_3$), 61.0 (d, C-1'), 86.1 (d, C-2'), 114.5 (d, C-3), 114.9 (s, CN), 124.5 (s, C-2), 126.2, 126.9, 128.2, 128.3, 128.4, 128.5 (d, Ar CH), 139.4, 140.2 (s, Ar C). Anal. C, H, N. *Z*-Isomer: an oil; $^{13}C$ NMR ($CDCl_3$) δ 11.5 (q), 33.3 (q), 36.0 (t), 56.9 (q), 64.1 (d), 85.3 (d), 116.6 (s), 124.8 (s), 126.4, 127.0, 127.6, 128.2, 128.5, 128.6 (d), 135.8 (d, C-3), 138.5, 140.0 (s). Anal. C, H, N.

By a similar procedure, equimolar amounts of 8, cinnamaldehyde, and KCN were dissolved in $CH_3CN$ and stirred for 4 h at room temperature to give 9 as a mixture of two C-2 epimers (1:1) in 90% yield. Attempts to separate the two epimers by chromatography on a silica gel column caused decomposition to give 8 and cinnamaldehyde.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-3-butenenitrile (3).** To an aqueous solution (8 mL) of L-ephedrine hydrochloride (2.02 g, 10 mmol) was added cinnamaldehyde (1.32 g, 1.26 mL, 10 mmol), followed by a saturated aqueous solution of KCN (0.65 g, 10 mmol). The solution was stirred at room temperature for about 20 min until it became turbid and contained yellow solids. $Et_2O$ (10 mL) was added, and the mixture was stirred for 3.5 h until the aqueous phase became clear. The aqueous layer was extracted with $Et_2O$, the combined $Et_2O$ solution was dried ($Na_2SO_4$) and filtered, and the filtrate was concentrated in vacuo to give 3 (2.48 g, 81% yield). The yellow moisture-sensitive crystals existed as a mixture of two C-2 epimers (1:1), mp 81–84 °C. Attempts to separate the two epimers of 3 by chromatography on a silica gel column or recrystallization from boiling MeOH caused decomposition to give cinnamaldehyde and ephedrine: IR (KBr) 3481 (OH), 2231 $cm^{-1}$ (CN); $^1H$ NMR ($CDCl_3$) δ 1.11 (1.5 H, d, *J* = 6.8 Hz, Me)/1.07 (1.5 H, d, *J* = 6.8 Hz), 2.48 (1.5 H, s, NMe)/2.38 (1.5 H, s), 2.94–3.06 (1 H, m, H-1'), 4.60 (0.5 H, dd, *J* = 4.4, 2.0 Hz, H-2)/4.74 (0.5 H, d, *J* = 4.4, 1.9 Hz), 4.86 (0.5 H, d, *J* = 10.4 Hz,

(21) (a) Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373. (b) Shirai, R.; Tanaka, M.; Koga, K. *J. Am. Chem. Soc.* **1986**, *108*, 543. (c) DePue, J. S.; Collum, D. B.; *J. Am. Chem. Soc.* **1988**, *110*, 5524. (d) Sato, D.; Kawasaki, H.; Shimada, I.; Arata, Y.; Okamura, K.; Date, T.; Koga, K. *J. Am. Chem. Soc.* **1992**, *114*, 761.

(22) (a) Meyers, A. I.; Beak, P. *Acc. Chem. Res.* **1986**, *19*, 356. (b) Fujisawa, T.; Funabora, M.; Ukaji, Y.; Sato, T. *Chem. Lett.* **1988**, 59.

(23) Yang, C. C.; Fang, J. M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3085.

H-2′)/4.97 (0.5 H, d, $J$ = 9.8 Hz), 5.88 (0.5 H, dd, $J$ = 16.0, 4.4 Hz, H-3)/5.98 (0.5 H, dd, $J$ = 16.0, 4.4 Hz), 6.85 (0.5 Hz, dd, $J$ = 16.0, 2.0 Hz, H-4)/6.82 (0.5 H, dd, $J$ = 16.0, 1.9 Hz), 7.24–7.41 (10 H, m).

**General Procedure for Reaction of 1–3 with Electrophiles.** To a cold (−78 °C) stirred solution of $i$-$Pr_2NH$ (0.4 mL, 2.4 mmol) in THF (2 mL) under $N_2$ was added dropwise $n$-BuLi (2.2 mmol, 1.37 mL of a 1.6 M in hexane). After 20 min, the resulting LDA solution was added via syringe dropwise into a cold (−78 °C) stirred solution of **3** (306 mg, 1 mmol) and LiI (1 mmol, 150 mg) in THF (3 mL) and HMPA (3 mmol, 0.54 mL). A solution of the appropriate electrophile (halide, aldehyde, 2-cyclohexenone, or methyl crotonate, 2 mmol) in THF (1 mL) was added dropwise. After being stirred for the specified time at the specified temperature (see Tables II and III), the reaction was quenched by addition of aqueous $NH_4Cl$. The mixture was concentrated, and the residue was taken up in EtOAc. The organic phase was washed with brine, dried ($Na_2SO_4$), and concentrated in vacuo to give the crude product. The ratio of isomers was analyzed by $^1H$ NMR spectroscopy. Separation of products was accomplished using silica gel columns and/or the HPLC. By using 1 equiv of LDA or $t$-BuOK (Table I), the reactions of **1** and **2** with electrophiles were conducted by similar procedures.

**2-(*N*-Methylanilino)-4-phenyl-2-butenenitrile (4).** *E*-Isomer: an oil; $^1H$ NMR ($CDCl_3$) $\delta$ 3.10 (3 H, s), 3.72 (2 H, d, $J$ = 8 Hz), 5.83 (1 H, t, $J$ = 7 Hz), 6.88–7.54 (10 H). *Z*-Isomer: an oil; $^1H$ NMR ($CDCl_3$) $\delta$ 3.07 (3 H, s), 3.44 (2 H, d, $J$ = 8 Hz), 6.36 (1 H, t, $J$ = 6 Hz), 6.66–7.44 (10 H).

**7-Chloro-2-(*N*-methylanilino)-4-phenyl-2-heptenenitrile (6).** *E*-Isomer: an oil; $^{13}C$ NMR ($CDCl_3$) $\delta$ 30.1 (t), 33.1 (t), 39.6 (q), 44.3 (t), 45.2 (d), 114.3 (s, CN), 120.0 (d, 2 C), 121.0 (s, C-2), 122.6 (d, C-3), 126.6 (d), 126.7 (d, 2 C), 128.6 (d, 2 C), 128.8 (d, 2 C), 132.5 (d), 142.3 (s), 145.9 (s). *Z*-Isomer: an oil; $^{13}C$ NMR ($CDCl_3$) $\delta$ 29.7 (t), 32.5 (t), 37.9 (q), 42.6 (t), 44.0 (d), 114.2 (d, 2 C), 115.6 (s), 118.9 (s), 119.7 (d), 126.7 (d), 127.1 (d, 2 C), 128.5 (d, 2 C), 128.9 (d, 2 C), 140.4 (s), 145.7 (s), 147.1 (d, C-3). Anal. C, H, N.

**5-(*o*-Bromophenyl)-2-(*N*-methylanilino)-4-phenyl-2-pentenenitrile (7).** *E*-Isomer: an oil; $^1H$ NMR ($CDCl_3$) $\delta$ 3.02 (3 H, s), 3.25 (1 H, dd, $J$ = 13.4, 9.9 Hz, H-5), 3.28 (1 H, dd, $J$ = 13.4, 5.7 Hz, H-5), 4.33 (1 H, m), 5.97 (1 H, d, $J$ = 11.0 Hz), 6.67–7.62 (14 H, m). *Z*-Isomer: an oil; $^1H$ NMR ($CDCl_3$) $\delta$ 2.63 (3 H, s), 3.14 (1 H, dd, $J$ = 13.4, 9.6 Hz), 3.21 (1 H, dd, $J$ = 13.4, 5.7 Hz), 4.33 (1 H, m), 6.65 (1 H, d, $J$ = 10.5 Hz), 6.42–7.57 (14 H, m). Anal. C, H, N.

**2-[*N*-Methyl-*N*-(2-methoxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2,6-heptadienenitrile (10).** Alkylation of the lithiated **2** with allyl bromide at room temperature for 5 h gave 50% of **10**, accompanied by 20% of the protonation product **2** with the *E*-configuration. The $\gamma$-substitution product **10** contained four isomers, (2*Z*,4*R*)/(2*Z*,4*S*)/(2*E*,4*R*)/(2*E*,4*S*) = 43:43:7:7, which were partially separated by chromatography. A mixture of 2*Z*,4*R*- and 2*Z*,4*S*-isomers (1:1): an oil; HPLC (EtOAc/hexane, 5:95) $t_R$ 5.6 min; $^{13}C$ NMR ($CDCl_3$, DEPT) $\delta$ 10.1 (C-3′)/14.1 (q), 32.2 ($NCH_3$)/36.6 (q), 40.8 (C-5)/41.1 (t), 42.6 (C-1′)/42.7 (d), 56.8 ($OCH_3$)/56.7 (q), 63.8 (C-4)/64.4 (d), 85.3 (C-2′)/85.4 (d), 116.8 (C-7)/117.0 (t), 124.2 (C-1)/124.4 (s), 126.7 (C-2)/126.7 (s), 135.1 (C-6)/135.2 (d), 139.4 (C-3)/140.7 (d), 128.7, 128.5, 128.4, 128.3, 127.4, 127.5 (d, Ar, CH)/126.7, 127.0, 127.4, 128.4, 128.6, 128.7 (d, Ar CH), 139.9, 142.2 (s, Ar C)/140.3, 142.2 (s, Ar C); HRMS ($C_{24}H_{28}N_2O$) requires 360.2202, found 360.2197. A mixture of 2*E*,4*R*- and 2*E*,4*S*-isomers (1:1): an oil; HPLC (EtOAc/hexane, 5:95) $t_R$ 5.2 min; HRMS found 360.2204.

**2-[*N*-Methyl-*N*-(2-methoxy-1-methyl-2-phenylethyl)amino]-4,5-diphenyl-2-pentenenitrile (11).** By using a base LDA, the lithiated **2** reacted with benzyl chloride (−78 °C to room temperature over 1 h) to give 50% of **11** containing four isomers, (2*Z*,4*R*)/(2*Z*,4*S*)/(2*E*,4*R*)/(2*E*,4*S*) = 33:14:29:24. If a base prepared from MeMgBr and $i$-$Pr_2NH$ was used instead of LDA, the reaction gave 38% of **11** containing two *E*-isomers, 4*R*/4*S* = 50:50. A mixture of 2*Z*,4*R*-, 2*Z*,4*S*-, 2*E*,4*R*-, and 2*E*,4*S*-isomers (33:14:29:24): an oil; $^1H$ NMR ($CDCl_3$) $\delta$ 0.86 (0.42 H, d, $J$ = 6.7 Hz, H-3′)/0.88 (1 H, d, $J$ = 5.9 Hz)/1.05 (0.97 H, d, $J$ = 6.8 Hz)/1.09 (0.72 H, d, $J$ = 6.9 Hz), 2.14 (0.42 H, s, $NCH_3$)/2.25 (1 H, s)/2.49 (0.87 H, s)/2.56 (0.72 H, s), 2.61–2.88 (1 H, m, H-1′), 2.90–3.13 (2 H, m, H-5), 3.18 (0.42 H, s, $OCH_3$)/3.19 (1 H, s)/3.23 (0.87 H, s)/3.24 (0.72 H, s), 3.99–4.29 (2 H, m, H-4), 5.88 (0.29 H, d, $J$ = 10.7 Hz, H-3)/5.93 (0.24 H, d, $J$ = 10.7 Hz)/6.14 (0.14 H, d, $J$ = 10.4 Hz)/6.23 (0.33 H, d, $J$ = 10.4 Hz), 6.73–7.39 (15 H, m, PhH); HRMS ($C_{28}H_{30}N_2O$) requires 410.2358, found 410.2377.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-butenenitrile (12).** *Z*-Isomer: pale yellow oil; TLC (EtOAc/hexane (15:85)) $R_f$ 0.25; $[\alpha]^{25}_D$ −5.0° ($CHCl_3$; $c$ = 3); $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.9 (q, C-3′), 33.2 (q, C-1″), 38.5 (t, C-4), 63.6 (d, C-1′), 73.5 (d, C-2′), 115.8 (s, C-1), 124.8 (s, C-2), 125.9 (d), 128.6 (d), 128.8 (d), 137.8 (s, Ar C), 139.7 (d, C-3), 141.0 (s, Ar C); HRMS ($C_{20}H_{22}N_2O$) requires 306.1733, found 306.1736. *E*-Isomer: yellow oil, TLC (EtOAc/hexane (15:85)) $R_f$ 0.28; $[\alpha]^{25}_D$ +59.0° ($CHCl_3$; $c$ = 6.93); $^{13}C$ NMR ($CDCl_3$) $\delta$ 12.4 (C-3′), 32.4 (C-1″), 35.7 (C-4), 61.3 (C-1′), 76.9 (C-2′), 115.0 (C-1), 115.4 (C-3), 124.4 (C-2), 126.5 (d), 126.7 (d), 127.3 (d), 127.6 (d), 127.9 (d), 128.8 (d), 140.1 (s), 142.1 (s); HRMS found 306.1739.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-pentenenitrile (13).** 2*Z*,4*R*-Isomer **13a**: an oil, HPLC (EtOAc/hexane (15:85)) $t_R$ 14 min; $[\alpha]^{25}_D$ −92.8° ($CHCl_3$; $c$ = 5); $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.9 (C-3′), 21.2 (C-5), 37.1 (C-1′), 39.5 (C-1″), 63.6 (C-4), 72.7 (C-2′), 115.5 (C-1), 123.1 (C-2), 125.8 (d), 126.8 (d), 126.9 (d), 127.2 (d), 128.2 (d), 129.0 (d), 141.0 (s), 143.3 (s), 146.7 (d, C-3). Anal. C, H, N. 2*E*,4*R*-Isomer **13b**: pale yellow crystal (from EtOAc/hexane): mp 87–88 °C; HPLC (EtOAc/hexane (15:85)) $t_R$ 18 min; $[\alpha]^{25}_D$ −7° ($CHCl_3$; $c$ = 5). Anal. C, H, N. 2*Z*,4*S*-Isomer **13c**: an oil, HPLC (EtOAc/hexane (15:85)) $t_R$ 16 min. 2*E*,4*S*-Isomer **13d**: pale yellow crystal from EtOAc/hexane; mp 72–73 °C; HPLC (EtOAc/hexane (15:85)) $t_R$ 20 min; $[\alpha]^{25}_D$ +136.8° ($CHCl_3$; $c$ = 8.75).

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-hexenenitrile (14).** 2*Z*,4*R*-Isomer **14a**: pale yellow oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 6 min; $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.7 (q), 12.0 (q), 29.4 (C-5), 39.2 (q), 44.8 (C-4), 63.6 (C-1′), 72.6 (C-2′), 115.5 (CN), 124.0 (C-2), 145.9 (C-3), 125.7, 126.7, 127.1, 127.3, 128.1, 141.0 (s), 142.2 (s); HRMS ($C_{22}H_{26}N_2O$) requires 334.2044, found 334.2047. 2*E*,4*R*-Isomer **14b**: an oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 9.6 min. 2*E*,4*S*-Isomer **14d**: an oil, HPLC (EtOAc/hexane (12:88)) $t_R$ 8.4 min.

**5-Methyl-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-hexenenitrile (15).** 2*Z*,4*R*-Isomer **15a**: an oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 4.4 min; $^1H$ NMR ($CDCl_3$) $\delta$ 0.75 (3 H, d, $J$ = 6.6 Hz), 0.87 (3 H, d, $J$ = 6.6 Hz), 0.94 (3 H, d, $J$ = 6.7 Hz), 1.90–1.97 (1 H), 2.44 (3 H, s), 2.83–2.90 (1 H, m), 3.62 (1 H, dd, $J$ = 9.6, 9.6 Hz), 4.84 (1 H, d, $J$ = 3 Hz), 6.36 (1 H, d, $J$ = 9.6 Hz), 7.12–7.41 (10 H); HRMS ($C_{23}H_{28}N_2O$) requires 348.2201, found 348.2193. An inseparable mixture of 2*E*,4*R*- and 2*E*,4*S*-isomers (1:1): HPLC (EtOAc/hexane (15:85)) $t_R$ 6.0 min; $^1H$ NMR ($CDCl_3$) $\delta$ 0.75 (d, $J$ = 6.7 Hz), 0.78 (d, $J$ = 6.6 Hz), 0.85 (d, $J$ = 6.7 Hz), 0.96 (d, $J$ = 6.7 Hz), 1.15 (d, $J$ = 6.7 Hz), 1.19 (d, $J$ = 6.7 Hz), 2.56 (s, H-1″), 3.28 (dd, H-4), 4.63 (d, $J$ = 5.6 Hz)/4.72 (d, $J$ = 5.6 Hz, H-2′), 5.08 (d, $J$ = 9.6 Hz, H-3).

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-octenenitrile (16).** 2*Z*,4*R*-Isomer **16a**: pale yellow oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 4.0 min; $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.7 (C-8), 13.8 (C-3′), 22.4 (C-7), 29.5 (C-6), 36.1 (C-5), 39.1 (C-1″), 43.2 (C-1′), 63.6 (C-4), 72.7 (C-2′), 115.6 (C-1), 123.8 (C-2), 125.7, 126.8, 127.1, 127.2, 128.1, 128.9, 141.1 (s), 142.5 (s), 145.9 (d, C-3); HRMS ($C_{24}H_{30}N_2O$) requires 362.2358, found 362.2359. An inseparable mixture of 2*E*,4*R*- and 2*E*,4*S*-isomers (2:1): HPLC (EtOAc/hexane (15:85)) $t_R$ 5.6 min.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2,6-heptadienenitrile (17).** 2*Z*,4*R*-Isomer **17a**: pale yellow oil; HPLC (EtOAc/hexane (13:87)) $t_R$ 6.8 min; $^1H$ NMR ($CDCl_3$) $\delta$ 0.91 (3 H, d, $J$ = 6.3 Hz), 2.28–2.47 (2 H), 2.51 (3 H, s), 2.93 (1 H, dq, $J$ = 6.3, 3.1 Hz), 4.04 (1 H, dt, $J$ = 10.1, 7.3 Hz), 4.85 (1 H, d, $J$ = 3.1 Hz), 4.96–5.14 (2 H), 5.57–5.70 (1 H), 6.22 (1 H, d, $J$ = 10.1 Hz), 7.17–7.57 (10 H). Anal. C, H, N. 2*E*,4*R*-Isomer **17b**: pale yellow oil; HPLC (EtOAc/hexane (13:87)) $t_R$ 10.4 min. 2*Z*,4*S*-Isomer **17c**: pale yellow oil; HPLC (EtOAc/hexane (13:87)) $t_R$ 7.8 min. 2*E*,4*S*-Isomer **17d**: pale yellow oil; HPLC (EtOAc/hexane (13:87)) $t_R$ 9.6 min.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4,5-diphenyl-2-pentenenitrile (18).** 2*Z*,4*R*-Isomer **18a**: colorless crystal; mp 89–92 °C (from EtOAc/hexane); HPLC (EtOAc/hexane (15:85)) $t_R$ 6.0 min; $^{13}C$ NMR ($CDCl_3$) $\delta$ 10.2 (C-

3′), 38.6 (C-1″), 43.1 (C-5), 45.3 (C-4), 63.5 (C-1′), 72.7 (C-2′), 115.4 (C-1), 124.3 (C-2), 126.5, 126.7, 127.1, 127.2, 128.1, 128.4, 128.9, 129.0, 138.6 (s), 141.1 (s), 144.4 (d, C-3). Anal. C, H, N. **2*E*,4*R*-Isomer 18b**: an oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 9.9 min. **2*E*,4*S*-Isomer 18d**: an oil, HPLC (EtOAc/hexane (15:85)) $t_R$ 9.7 min.

**5-(2-Bromophenyl)-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-pentenenitrile (19).** **2*Z*,4*R*-Isomer 19a**: an oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 6.2 min; $^1$H NMR ($CDCl_3$) $\delta$ 0.62 (3 H, d, $J$ = 6.7 Hz, H-3′), 2.22 (3 H, s, $NCH_3$), 2.77 (1 H, dq, $J$ = 6.7, 3.3 Hz, H-2′), 3.07 (1 H, dd, $J$ = 13.3, 9.8 Hz, H-5), 3.19 (1 H, dd, $J$ = 13.3, 5.7 Hz, H-5), 4.54–4.66 (1 H, m, H-4), 4.80 (1 H, d, $J$ = 3.3 Hz, H-1′), 6.38 (1 H, d, $J$ = 10.1 Hz, H-3), 7.00–7.07 (2 H, m), 7.13–7.35 (12 H, m, ArH), 7.55 (1 H, d, $J$ = 8.0 Hz); HRMS ($C_{27}H_{28}N_2O^{79}Br$) requires 475.1385, found 475.1344. **2*E*,4*R*-Isomer 19b**: an oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 6.8 min; HRMS found 477.1351. **2*Z*,4*S*-Isomer 19c**: an oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 6.5 min. **2*E*,4*S*-Isomer 19d**: an oil; HPLC (EtOAc/hexane (12:88)) $t_R$ 7.6 min.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-(phenylthio)-2-butenenitrile (20).** **2*Z*,4*R*-Isomer 20a**: an oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 5.2 min; $^1$H NMR ($CDCl_3$) $\delta$ 0.94 (3 H, d, $J$ = 6.5 Hz, H-3′), 2.26 (3 H, s, $NCH_3$), 2.92–2.96 (1 H, m, H-1′), 4.72 (1 H, d, $J$ = 3.4 Hz, H-2′), 5.33 (1 H, d, $J$ = 11.2 Hz, H-4), 6.28 (1 H, d, $J$ = 11.2 Hz, H-3), 7.12–7.48 (15 H, m, ArH). **2*E*,4*R*-Isomer 20b**: an oil, HPLC (EtOAc/hexane (15:85)) $t_R$ 6.8 min. **2*Z*,4*S*-Isomer 20c**: an oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 5.0 min. **2*E*,4*S*-Isomer 20d**: an oil; HPLC (EtOAc/hexane (15:85)) $t_R$ 6.2 min.

**Hydrolysis of 13–19 to Carboxylic Acids 21–26.** The starting material (1 mmol, 13–19) was dissolved in THF (3 mL) and aqueous oxalic acid (3 mL of 30% solution). The mixture was heated (100 °C oil bath) at reflux for 12 h, cooled, and concentrated in vacuo. The residue was treated with aqueous KOH (10% solution) to pH 12, and the neutral compound was extracted with EtOAc. The aqueous phase was acidified with aqueous HCl (3 N) to pH 2 and extracted three times with EtOAc, and the combined extracts were concentrated in vacuo to give the corresponding carboxylic acid (21–26).

**3-Phenylbutanoic acid (21)**: *R*-isomer, $[\alpha]^{25}_D$ −57.1° (PhH; $c$ = 5) [lit.[14a] $[\alpha]^{25}_D$ −57.23° (PhH; $c$ = 5)]; *S*-isomer, $[\alpha]^{25}_D$ +57.6° (PhH; $c$ = 1) [lit.[14e] $[\alpha]^{25}_D$ +57.99° (PhH; $c$ = 5)].

**3-Phenylpentanoic acid (22)**: *R*-isomer, $[\alpha]^{25}_D$ −45.3° (PhH; $c$ = 0.4) [lit.[14f] $[\alpha]^{25}_D$ −49.5° (PhH; $c$ = 7.11)].

**4-Methyl-3-phenylpentanoic acid (23)**: *R*-isomer, mp 39–40 °C; $[\alpha]^{25}_D$ −35.5° ($CHCl_3$; $c$ = 0.75).

**3-Phenylheptanoic acid (24)**: *R*-isomer, $[\alpha]^{25}_D$ −28.3° (PhH; $c$ = 0.8) [lit.[14c,e] $[\alpha]^{25}_D$ −34.4° (PhH; $c$ = 8.12)].

**3-Phenyl-5-hexenoic acid (25)**: *R*-isomer, $[\alpha]^{25}_D$ −10.5° ($CH_3OH$; $c$ = 1.33); IR (neat) 3026–2500 (br, OH), 1706 (C=O) cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.38 (2 H, dd, $J$ = 15.8, 8.4 Hz, H-4), 2.58 (1 H, dd, $J$ = 15.8, 8.4 Hz, H-2), 2.71 (1 H, dd, $J$ = 15.8, 8.4 Hz), 2.71 (1 H, dd, $J$ = 15.8, 6.2 Hz, H-2), 3.13–3.23 (1 H, m, H-3), 4.97 (1 H, dd, $J$ = 9.9, 3.4 Hz, H-6), 5.00 (1 H, m, H-5), 6.94 (br s, COOH), 7.16–7.30 (5 H, m, PhH).

**3,4-Diphenylbutanoic acid (26)**: *R*-isomer, mp 99–101 °C (15:85 EtOAc/*n*-hexane); $[\alpha]^{25}_D$ +52° (PhH; $c$ = 0.85) [lit.[14b] $[\alpha]$ +59° (PhH; $c$ = 1.85)].

**5-Hydroxy-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-2-heptenenitrile (27).** An inseparable mixture of **2*Z*,4*R*,5*S*-**, **2*Z*,4*R*,5*R*-**, and **2*Z*,4*S*,5*R*-isomers (a/b/c = 67:22:11): HPLC (EtOAc/hexane (18:82)) $t_R$ 14.2 min. **2*Z*,4*S*,5*S*-Isomer d**: HPLC (EtOAc/hexane (18:82)) $t_R$ 14.3 min. **2*E*,4*R*,5*R*-Isomer f**: HPLC (EtOAc/hexane (18:82)) $t_R$ 13.8 min; $^1$H NMR ($CDCl_3$) $\delta$ 0.92 (6 H, t, $J$ = 6.4 Hz), 1.22–1.32 (2 H, m), 2.40 (3 H, s), 2.88 (1 H, dq, $J$ = 1.8, 6.4 Hz), 3.61 (1 H, dt, $J$ = 8.2, 3.4 Hz), 4.15 (1 H, t, $J$ = 10.1 Hz), 4.94 (1 H, d, $J$ = 8 Hz), 5.93 (1 H, d, $J$ = 10.1 Hz), 7.09 (d, $J$ = 7.3 Hz), 7.25–7.42 (8 H); HRMS ($C_{23}H_{28}N_2O_2$) requires 364.2151, found 364.2181.

**5-Hydroxy-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4,5-diphenyl-2-pentenenitrile (28).** **2*Z*,4*R*,5*R*-Isomer a**: an oil; TLC (EtOAc/hexane (15:85)) $R_f$ 0.15; $^{13}$C NMR ($CDCl_3$) $\delta$ 10.5 (C-3′), 39.3 ($NCH_3$), 50.5 (C-2), 63.2 (C-4), 72.8 (C-2′), 77.7 (C-5), 115.3 (CN), 125.6 (d), 125.8 (d), 126.8 (d), 127.1 (d), 127.6 (d), 128.1 (d), 128.2 (d), 128.6 (d), 128.8 (d), 138.1 (s), 139.8 (s), 140.7 (s), 141.1 (C-3); HRMS ($C_{27}H_{28}N_2O_2$) requires 412.2151, found 412.2125. **2*Z*,4*R*,5*S*-Isomer b**: an oil, TLC (EtOAc/hexane (15:85)) $R_f$ 0.25. **2*Z*,4*S*,5*R*-Isomer d**: an oil; TLC (EtOAc/hexane (15:85)) $R_f$ 0.20; HRMS found 412.2126.

**5-Hydroxy-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-phenyl-5-(4-bromophenyl)-2-pentenenitrile (29).** **2*Z*,4*R*,5*R*-Isomer a**: an oil; HPLC (EtOAc/hexane (27:73)) $t_R$ 10.9 min. **2*Z*,4*R*,5*S*-Isomer b**: an oil; HPLC (EtOAc/hexane (27:73)) $t_R$ 9.8 min; $[\alpha]^{25}_D$ = +8.7° ($CHCl_3$; $c$ = 2.5); $^1$H NMR ($CDCl_3$) $\delta$ 0.83 (3 H, d, $J$ = 6.6 Hz), 2.26 (3 H, s), 2.91 (1 H, dq, $J$ = 1.9, 6.6 Hz), 3.23 (1 H, br s, OH), 4.56 (1 H, dd, $J$ = 5.8, 10.9 Hz), 5.16 (2 H, d, $J$ = 5.8 Hz), 6.21 (1 H, d, $J$ = 10.9 Hz), 6.89 (2 H, d, $J$ = 8.2 Hz), 7.03 (2 H, d, $J$ = 8.2 Hz), 7.21–7.39 (14 H, m); HRMS ($C_{27}H_{28}N_2O_2{}^{79}Br$) requires 491.1320, found 491.1292. **2*Z*,4*S*,5*R*-Isomer d**: an oil; HPLC (EtOAc/hexane (27:73)) $t_R$ 8.4 min; $[\alpha]^{25}_D$ = −1.1° ($c$ = 0.75, $CHCl_3$); HRMS found 491.1326. **2*E*,4*R*,5*S*-Isomer f**: an oil; HPLC (EtOAc/hexane (27:73)) $t_R$ 7.0 min; $[\alpha]^{25}_D$ = +54.2° ($CHCl_3$; $c$ = 0.33).

**Hydrolysis of 27–29 to Lactones 30–32.** The starting material (1 mmol, 27–29) was dissolved in THF (3 mL) and aqueous oxalic acid (3 mL of 30% solution). The mixture was heated (100 °C oil bath) at reflux for 12 h, cooled, and concentrated in vacuo. The residue was partitioned between brine and EtOAc. The aqueous phase was separated and extracted with EtOAc. The combined organic phase was dried ($Na_2SO_4$) and filtered. The filtrate was concentrated, and the residue was chromatographed on a silica gel column (EtOAc/hexane (15:85)) to give the corresponding lactone (30–32).

**5-Ethyl-4-phenyltetrahydrofuran-2-one (30).** **4*R*,5*S*-Cis-isomer**: $[\alpha]^{25}_D$ +58.6° ($CHCl_3$; $c$ = 0.5); IR (neat) 1778 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.88 (3 H, t, $J$ = 7.5 Hz), 1.16–1.32 (2 H, m), 2.74 (1 H, m), 2.92 (1 H, m), 3.72 (1 H, m), 4.61 (1 H, m), 7.24 (5 H, m). **4*R*,5*R*-Trans-isomer**: $^1$H NMR ($CDCl_3$) $\delta$ 0.98 (3 H, t, $J$ = 7.5 Hz), 1.62–1.80 (2 H, m), 2.74 (1 H, dd, $J$ = 17.7, 10.3 Hz), 2.92 (1 H, dd, $J$ = 17.7, 8.6 Hz), 3.27 (1 H, m), 4.37 (1 H, m), 7.25 (5 H, m). Anal. C, H.

**4,5-Diphenyltetrahydrofuran-2-one (31).** **4*R*,5*R*-Cis-isomer a**: mp 90–92 °C; $[\alpha]^{25}_D$ +48° ($CHCl_3$; $c$ = 1); CD ($CH_3CN$) $[\theta]_{225}$ 2777, $[\theta]_{222}$ 0, $[\theta]_{221.5}$ −1263, $[\theta]_{220}$ 0, $[\theta]_{217.5}$ 2050, $[\theta]_{216}$ 0, $[\theta]_{215.5}$ −191; $^1$H NMR ($CDCl_3$) $\delta$ 2.89 (1 H, dd, $J$ = 17.0, 6.6 Hz), 3.05 (1 H, dd, $J$ = 17.0, 8.1 Hz), 4.05 (1 H, m), 5.81 (1 H, d, $J$ = 6.6 Hz), 6.76–6.92 (4 H), 7.06–7.26 (6 H, m). **4*R*,5*S*-Trans-isomer b**: mp 100–102 °C; $[\alpha]^{25}_D$ +30.3° ($CHCl_3$, $c$ = 1.34). Anal. C, H. **4*S*,5*R*-Trans-isomer d**: $[\alpha]^{25}_D$ −30.3° ($CHCl_3$, $c$ = 1.34); CD ($CH_3CN$) $[\theta]_{224.3}$ −1075, $[\theta]_{220.5}$ −49 380, $[\theta]_{214.5}$ 0, $[\theta]_{213.2}$ 2645.

**5-(4-Bromophenyl)-4-phenyltetrahydrofuran-2-one (32).** **4*R*,5*R*-Cis-isomer a**: TLC (EtOAc/hexane (15:85)) $R_f$ 0.18; $[\alpha]^{25}_D$ −30.3° ($c$ = 2.5, $CHCl_3$); CD ($CH_3CN$) $[\theta]_{253.5}$ −3630, $[\theta]_{232.0}$ −229, $[\theta]_{226.5}$ 1488, $[\theta]_{222.5}$ −151; HRMS ($C_{16}H_{13}O_2{}^{79}Br$) requires 316.0098, found 316.0097. **4*R*,5*S*-Trans-isomer b**: TLC (EtOAc/hexane (15:85)) $R_f$ 0.24; $[\alpha]^{25}_D$ −46.3° ($c$ = 0.5, $CHCl_3$); CD ($CH_3CN$) $[\theta]_{248.5}$ −1708, $[\theta]_{235.0}$ 32 760, $[\theta]_{224.0}$ 124 300, $[\theta]_{212.5}$ −5282. **4*S*,5*R*-Trans-isomer d**: $[\alpha]^{25}_D$ +42.6° ($c$ = 1.0, $CHCl_3$); CD ($CH_3CN$) $[\theta]_{248.5}$ −4512, $[\theta]_{235.0}$ −34 300, $[\theta]_{224.0}$ −124 600, $[\theta]_{212.5}$ −6193.

**2-[*N*-Methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-4-(3-oxocyclohexyl)-4-phenyl-2-butenenitrile (33).** A mixture containing two *E*-isomers and two *Z*-isomers (a/b/c/d = 36:36:18:10): TLC (EtOAc in hexane (30:70)) $R_f$ 0.23; $^1$H NMR ($CDCl_3$) $\delta$ 1.20/0.92/0.88 (d, $J$ = 6.7 Hz, Me), 1.30–1.65 (2 H, m), 1.81–2.15 (5 H, m), 2.21–2.36 (2 H, m), 2.56/2.64/2.44/2.43 (s, NMe), 3.28–3.46 (1 H, m), 3.68–4.04 (1 H, m), 4.82 (br s)/4.80 (br s)/4.57 (br s)/4.70 (br s, H-2′), 4.90 (d, $J$ = 10.7 Hz)/4.62 (d, $J$ = 9.4 Hz)/6.25 (d, $J$ = 10.2 Hz)/6.18 (d, $J$ = 10 Hz, H-3), 7.03–7.34 (10 H, m); HRMS ($C_{26}H_{30}N_2O_2$) requires 402.2308, found 402.2296.

**Methyl 6-Cyano-6-2-[*N*-methyl-*N*-(2-hydroxy-1-methyl-2-phenylethyl)amino]-3-methyl-4-phenyl-5-hexenoate (34).** A mixture of two isomers a/b (2:1): $^{13}$C NMR ($CDCl_3$) $\delta$ 12.3/12.7, 17.6, 32.5, 35.9/36.0, 39.5 (NMe), 51.4/52.0, 61.2/61.3, 76.6, 114.8/114.9 (CN), 117.2, 118.1, 124.3, 124.4, 126.0, 126.1, 126.6, 127.6, 127.6, 127.8, 128.0, 128.3, 128.7, 141.8, 142.1, 142.9, 143.1, 173.3/173.4 (C=O); HRMS ($C_{25}H_{30}N_2O_3$) requires 406.2257, found 406.2218. A mixture of two isomers c/d (2:1): $^{13}$C NMR ($CDCl_3$) $\delta$ 12.4/13.0, 18.4, 32.3, 36.1, 39.6/39.9 (NMe), 51.5, 52.9, 61.2, 83.7, 114.8 (CN), 117.2, 118.1, 121.4, 124.2, 125.6, 125.9, 126.2, 126.5, 127.5, 127.6, 127.9, 128.3, 128.5, 128.6, 141.8, 142.1, 143.0, 143.2, 173.7 (C=O).

**Conversion of γ-Lactone 30a to (*R*)-3-Phenylhexanol and (*S*)-3-Phenylhexane.** To a solution of the trans-γ-lactone **30a** (48 mg, 0.2 mmol) in THF (3 mL) was added $BH_3$·$SMe_2$ (0.5 mL of a 2 M solution in $Et_2O$), and the mixture was heated (100 °C oil bath) under reflux for 2 h. The solution was cooled and treated with several drops of a mixture of glycerin/$H_2O$/THF (1:1:1) and heated under reflux for an additional 30 min. The mixture was concentrated in vacuo, and the residue was partitioned between brine and EtOAc. The organic phase was dried ($Na_2SO_4$) and filtered, and the filtrate was concentrated in vacuo to give a 94% yield of (3*R*,4*R*)-*trans*-3-phenyl-1,4-hexanediol (36 mg). The diol (27 mg, 0.15 mmol) was dissolved in cold (0 °C) anhydrous $CH_2Cl_2$ (3 mL), and $Et_3N$ (0.15 mL, 1.5 mmol) and MsCl (0.1 mL, 1.1 mmol) were subsequently added. The mixture was stirred at 0 °C for 45 min and quenched by addition of ice. The organic phase was separated and washed with saturated aqueous $NaHCO_3$ and 10% aqueous $NaH_2PO_4$. The organic phase was dried ($Na_2SO_4$) and filtered, and the filtrate was concentrated in vacuo to give the corresponding dimesylate (42 mg, 85%). The dimesylate (42 mg, 0.13 mmol) was dissolved in THF (3 mL) and treated with $LiAlH_4$ (20 mg, 0.3 mmol). After the solution was stirred at room temperature for 48 h, an (*R*)-3-phenylhexanol was obtained (18 mg, 78%). If the mixture was heated (100 °C oil bath) under reflux for 24 h, an (*S*)-3-phenylhexane was obtained (13 mg, 62%). By similar procedures, both the cis lactone **31a** and its trans isomer **31b** were converted to an (*S*)-1,2-diphenylbutane. Both the cis and trans lactones **32a** and **32b** were converted to an (*S*)-1-(4-bromophenyl)-2-phenylbutane.

**(*R*)-3-Phenylhexanol**: a liquid; $[\alpha]^{25}_D$ −3.5° ($CHCl_3$; *c* = 0.1) [lit.[16] $[\alpha]^{25}_D$ −6.47°].

**(*S*)-3-Phenylhexane**: a liquid; $[\alpha]^{25}_D$ −0.6° ($CHCl_3$; *c* = 0.5) [lit.[16] $[\alpha]^{25}_D$ −1.09° (neat)].

**(*S*)-1,2-Diphenylbutane**: a liquid; $[\alpha]^{25}_D$ +12.5° ($CHCl_3$; *c* = 0.3).

**(*S*)-1-(4-Bromophenyl)-2-phenylhexane**: a liquid; $[\alpha]^{25}_D$ +13.3° ($CHCl_3$; *c* = 0.2).

**Acknowledgment.** We are grateful to Professor Yu Wang (Department of Chemistry, National Taiwan University) for the X-ray measurement and to the National Science Council for financial support (Grant NSC 81-0208-M002-20).

**Supplementary Material Available:** NMR spectra and additional spectral data of new compounds (32 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.