# Diels−Alder Reaction of Heterocyclic Imine Dienophiles

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The stereoselective aza-Diels−Alder reaction is one of the most important methods for the synthesis of nitrogen-containing bicyclic structures.[1] These products are in turn highly useful for the synthesis of many natural products and have recently also found use as precursors for chiral ligands in catalytic asymmetric synthesis. We have been specially interested in the diastereoselective aza-Diels−Alder reaction between cyclopentadiene and chiral glyoxylate-derived imines.[2] A wide variety of derivatives of these adducts (Figure 1) have been successfully used as chiral ligands and synthetic precursors.[3] A major drawback of this reaction is its narrow scope, and apparently the aldehyde must be either an electron-deficient glyoxylate aldehyde[2] or a very small one, e.g., formaldehyde.[4]

Since the isolation of epibatidine (**1**) (Figure 2) in 1992,[5] a great deal of work has been devoted to the alkaloid, either on its direct synthesis[6] or in the preparation of analogues[7] that might have high(er) analgesic activity and/or lower toxicity than epibatidine itself. Recently a number of structures having the nitrogen in various positions of the norbornane framework have been published, and one example in which the nitrogen is located next to the pyridine ring (**2**) has shown promising activity.[8] Pharmaceutically this might be an interesting class of compounds, since they can be viewed as bicyclic nicotine (**3**) analogues.[9]

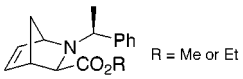



**Figure 1.** The aza-Diels−Alder adduct.

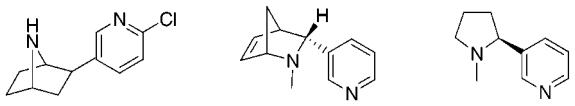
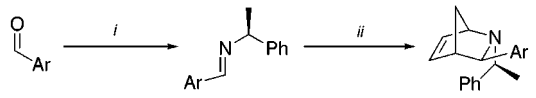



**Figure 2.** Some biologically active compounds.

**Scheme 1. Aza-Diels−Alder Reaction**[a]




[a] Key: (*i*) (*S*)-1-phenylethylamine, MS 4 Å, $CH_2Cl_2$, rt; (*ii*) acid(s), cyclopentadiene, −78 °C to room temperature.

## Results and Discussion

The cycloaddition between the glyoxylate imines and cyclopentadiene is highly accelerated by the addition of a Brønsted acid and a Lewis acid. This results in the formation of a protonated iminium cation complex that rapidly undergoes [4 + 2] cycloaddition with dienes even at very low temperatures.[2a] It occurred to us that the presence of a second nitrogen, if being placed in conjugation with the imine, might fulfill the role as an electron-withdrawing group under the acidic reaction conditions. Indeed, when pyridine-2-carboxaldehyde (**4a**) was consequently treated with (*S*)-1-phenylethylamine and cyclopentadiene under acidic conditions, a highly stereoselective cycloaddition took place, giving the pyridine-substituted aza-norbornene (**5a**) in good yield (Scheme 1).

The choice of acid proved to be important for the outcome of the reaction. The use of a Lewis acid such as borontriflouride, which is beneficial in the corresponding cycloaddition of glyoxylate-derived imines, only resulted in a fast polymerization of the aldehyde. On the other hand, strong Brønsted acids such as methane sulfonic acid and triflouroacetic acid proved to be effective for the desired purpose, and the use of either alone or in a 1:1 combination resulted in good conversion and stereoselectivity for the reaction. The relative rate between polymerization and cycloaddition was found to be temperature-dependent, and performing the reactions at lower temperatures suppressed the unwanted polymerization to a minimum. All reactions were thereafter performed at −78 °C, allowing the reaction to slowly reach room temperature overnight. The workup consisted of quenching the acid(s) by either addition of sodium bicarbonate or sodium hydroxide solutions and extrac-

(1) *Hetero Diels−Alder Methodology in Organic Synthesis*; Academic Press: London, 1987; Chapter 2.

(2) (a) Stella, L.; Abraham, H.; Feneu-Dupont, J.; Tinant, B.; Declercq, J. P. *Tetrahedron Lett.* **1990**, *31*, 2063. (b) Waldmann, H.; Braun, M. *Liebigs Ann. Chem.* **1991**, 1045. (c) Bailey, P. D.; Wilson, R. D.; Brown, G. R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1337. (d) Bailey, P. D.; Brown, G. R.; Korber, F.; Reed, A.; Wilson, R. D. *Tetrahedron: Asymmetry* **1991**, *2*, 1263. (e) Abraham, H.; Stella, L. *Tetrahedron* **1992**, *48*, 9707. (f) Bailey, P. D.; Londesbrough, D. J.; Hancox, T. C.; Hefferman, J. D.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1994**, 2543. (g) Bailey, P. D.; Millwood, P. A.; Smith, P. D. *Chem. Commun.* **1998**, 633.

(3) (a) For a review on our work with 2-azanorbornyl structures, see: Brandt, P.; Andersson, P. G. *Synlett* **1999**, accepted for publication. (b) Nakano, H.; Kumagai, N.; Kabuto, C.; Matsuzaki, H.; Hongo, H. *Tetrahedron: Asymmetry* **1995**, *6*, 1233. (c) Nakano, H.; Kumagai, N.; Matsuzaki, H.; Kabuto, C.; Hongo, H. *Tetrahedron: Asymmetry* **1997**, *44*, 435. (d) Nakano, H.; Iwasa, K.; Hongo, H. *Heterocycles* **1997**, 2085. (e) Kobayashi, T.; Ono, K.; Kato, H. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 61. (f) Ward, S. E.; Holmes, A. B.; McCague, R. *Chem. Commun.* **1997**, 2085.

(4) Larsen, S. D.; Grieco, P. A. *J. Am. Chem. Soc.* **1985**, *107*, 1768.

(5) Spande, T. F.; Garraffo, H. M.; Edwards, M. W.; Yeh, H. J. C.; Pannell, L.; Daly, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 3475.

(6) (a) Structure assignment of epibatidine: Broka, C. *Med. Chem. Res.* **1994**, *4*, 449. (b) First synthesis of racemic epibatidine: Broka, C. A. *Tetrahedron Lett.* **1993**, *34*, 3251. (c) As an example of a asymmetric synthesis of the alkaloid and for a general overview of its synthesis, see: Aoyagi, S.; Tanaka, R.; Naruse, M.; Kibayashi, C. *J. Org. Chem.* **1998**, *63*, 8397 and references therein. (d) For a recent synthesis of epibatidine, see: Hall, A.; Bailey, P. D.; Rees, D. C.; Wightman, R. H. *Chem. Commun.* **1998**, 2251. (e) Palmgren, A.; Larsson, A.; Bäckvall, J. E.; Halquist, P. *J. Org. Chem.* **1999**, *64*, 836.

(7) See, for example: (a) Malpass, J. R.; Hemmings, D. A.; Wallis, A. L. *Tetrahedron Lett.* **1996**, *37*, 3911. (*b*) Zhang, C.; Gyermek, L.; Trudell, M. L. *Tetrahedron Lett.* **1997**, *38*, 5619. (*c*) Hodgson, D. M.; Maxwell, I. R. *Synlett* **1998**, 1349. (*d*) Malpass, J. R.; Cox, C. D. *Tetrahedron Lett.* **1999**, *40*, 1419.

(8) Bencherif, M.; Caldwell, W. S.; Dull, G. M.; Lippielo, P. M. Pharmaceutical Compositions for the Treatments of Central Nervous System Disorders. U.S. Patent 5,583,140, 1996.

(9) For a review on nicotine and related drugs, see: Holladay, M. W.; Dart, M. J.; Lynch, J. K. *J. Med. Chem.* **1997**, *40*, 4169.

10.1021/jo9916683 CCC: $19.00 
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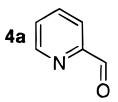
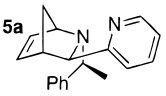
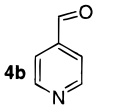
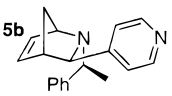
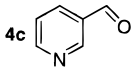
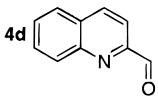
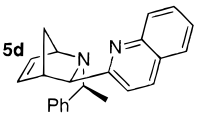
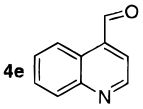
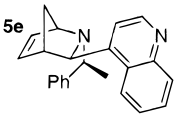
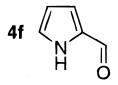
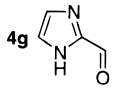
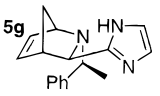
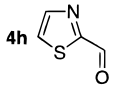
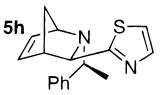
**Table 1. Cycloaddition Results**

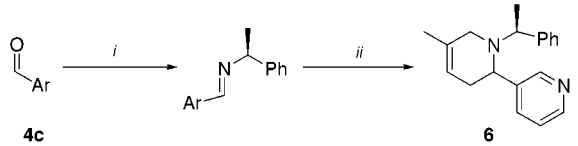
| Entry | Aldehyde[a] | Reaction conditions | Yield[b] | *exo*/*endo* selectivity[c] | Diastereosectivity[d] | Product |
|---|---|---|---|---|---|---|
| 1 | **4a**  | $CH_3SO_3H$ / TFA | 80 | > 99 % | 87:13 | **5a**  |
| 2 | **4b**  | $CH_3SO_3H$ / TFA | 60 | > 99 % | 80:20 | **5b**  |
| 3 | **4c**  | $CH_3SO_3H$ / TFA or $CH_3SO_3H$ | --- | --- | *e* | --- |
| 4 | **4d**  | $CH_3SO_3H$ | 80 | > 99 % | 90:10 | **5d**  |
| 5 | **4e**  | $CH_3SO_3H$ | 79 | > 99 % | 90:10 | **5e**  |
| 6 | **4f**  | $CH_3SO_3H$ / TFA or $CH_3SO_3H$ | --- | --- | *e* | --- |
| 7 | **4g**  | $CH_3SO_3H$ | 60 | > 99 % | 75:25 | **5g**  |
| 8 | **4h**  | $CH_3SO_3H$ | 80 | > 99 % | 90:10 | **5h**  |

[a] All aldehydes were used as received from the commercial sources. [b] Refers to the isolated yield over the two isomers. [c] No *endo* isomer could be observed. [d] Determined by integration of the signals on the crude $^1$H NMR. [e] The imine of the corresponding aldehyde was formed, but no Diels−Alder reaction occurred.

tion. The major isomer was then isolated by means of chromatography in good yield. The reaction proved to be successful for a wide variety of heterocyclic aromatic aldehydes listed in Table 1 together with the appropriate reaction conditions.

As expected, pyridine-3-carboxaldehyde (**4c**, entry 3, Table 1) and pyrrrole-2-carboxaldehyde (**4f**, entry 6, Table 1) failed to react in a Diels−Alder fashion, even though the corresponding imines could be formed. This clearly shows the importance of having a second nitrogen in conjugation with the imine and clearly defines the scope of the reaction. Isoprene could be used instead of cyclopentadiene, but the cycloaddition required a more active Lewis acid.[11] One should notice, however, that the reaction with isoprene was successful when using pyridine-3-carboxaldehyde imine (Scheme 2). Because pyridine is a very good ligand for a variety of metals, we believe that some of these epibatidine analogues will also find use as chiral ligands in catalytic asymmetric synthesis. The extension of the aza-Diels−Alder reaction to other aldehydes and further application of these compounds in catalysis, synthesis, and in vitro testing are currently under investigation and will be reported in due time.

**Scheme 2. Use of Isoprene[a]**



**4c** **6**

[a] Key: (*i*) (*S*)-1-phenylethylamine, MS 4 Å, $CH_2Cl_2$, rt; (*ii*) $ZnCl_2$, isoprene, $CH_2Cl_2$/ether, rt.

## Experimental Section

For general experimental information see ref 10. All aldehydes were used as received from the commercial suppliers, as were (*S*)-1-phenylethylamine and the acids. Cyclopentadiene was

(10) Bedekar, A. V.; Koroleva, E. B.; Andersson, P. G. *J. Org. Chem.* **1997**, *62*, 2518.

(11) Pfrengle, W.; Kunz, H. *J. Org. Chem.* **1989**, *54*, 4263. See synthesis of compound **6** for a representative procedure. The absolute stereochemistry of the major isomer has not been determined.

distilled just prior to use. The stereochemistry of compounds **5** was assigned by means of NOESY experiments.

**General Procedure for the Aza-Diels−Alder Reactions.** A round-bottom flask containing 4 Å MS (2 g) was placed under argon, and dry $CH_2Cl_2$ (20 mL) added. To the stirring suspension was then added via syringe the desired aldehyde (10 mmol) and (*S*)-1-phenylethylamine (1 equiv in relation to the aldehyde). The reaction was allowed to stir at room temperature until the imine formation was complete (according to $^1$H NMR). The mixture was than cooled to −78 °C using an acetone/dry ice bath, and the acid(s) was added (2 equiv in relation to the imine), followed by addition of freshly distilled cyclopentadiene (1.4 equiv in relation to the imine). The reaction was afterward stirred overnight and allowed to slowly reach room temperature. The mixture was then quenched by the addition of saturated $NaHCO_3$ solution or a 20% solution of NaOH. Extraction and solvent evaporation afforded a residue that was purified by means of preparative HPLC on a C-18 column using MeOH/$H_2O$ (70:30) as eluent.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(2-pyridyl)hept-5-ene (5a).** Conversion of the aldehyde into the corresponding imine was achieved after 1 h. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a white solid: mp 82−83 °C; $[\alpha]^{24}_D$ +194.5 (*c* 2.4, $CH_2Cl_2$); IR ($CH_2Cl_2$, cm$^{-1}$) 2875, 1952, 1588, 1571, 1494 and 1097; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.35 (1H, d, $J$ = 8.4 Hz), 1.47 (3H, d, $J$ = 6.4 Hz), 1.96 (1H, d, $J$ = 8.4 Hz), 2.83 (1H, br s), 2.94 (1H, s), 3.19 (1H, q, $J$ = 6.4 Hz), 4.35 (1H, br s), 6.26−6.35 (1H, m), 6.82−7.00 (1H, m), 7.10−7.19 (2H, m), 7.29−7.39 (2H, m) and 8.27−8.30 (1H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 21.8, 43.9, 51.2, 63.2, 63.7, 68.6, 120.5, 122.6, 126.4, 127.4, 128.1, 132.1, 135.1, 137.3, 144.6, 148.0 and 163.8; MS (EI) *m*/z (rel intensity) 276 (M$^+$, <1%), 196 (14), 195 (100), 105 (12) and 79 (12). Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.13. Found: C, 82.71; H, 7.42; N, 9.87.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(4-pyridyl)hept-5-ene (5b).** Conversion of the aldehyde into the corresponding imine was achieved after 1 h. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a pale yellow oil: $[\alpha]^{24}_D$ +154.7 (*c* 4.4, $CH_2Cl_2$); IR ($CH_2Cl_2$, cm$^{-1}$) 2875, 1598, 1493 and 1102; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.34 (1H, d, $J$ = 8.4 Hz), 1.45 (3H, d, $J$ = 6.4 Hz), 1.82 (1H, d, $J$ = 8.4 Hz), 2.61 (1H, br s), 2.75 (1H, s), 3.13 (1H, q, $J$ = 6.4 Hz), 4.33 (1H, br s), 6.28−6.33 (1H, m), 6.50 − 6.60 (1H, m), 6.90−7.18 (7H, m) and 8.23−8.30 (2H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 21.9, 43.7, 52.3, 63.1, 63.7, 66.5, 122.7, 122.8, 126.8, 127.6, 128.1, 132.5, 136.8, 148.3 and 148.6; MS (EI) *m*/z (rel intensity) 276 (M$^+$, <1%), 210 (26), 209 (21), 183 (52), 106 (37), 105 (100) and 103 (15). Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.13. Found: C, 82.60; H, 7.18; N, 10.22.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(2-quinolyl)hept-5-ene (5d).** Conversion of the aldehyde into the corresponding imine was achieved after stirring overnight at room temperature. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a yellow oil: $[\alpha]^{24}_D$ +94.5 (*c* 1.3, $CH_2Cl_2$); IR ($CH_2Cl_2$, cm$^{-1}$) 2860, 1973, 1546, 1522, 1455 and 1138; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.36 (1H, d, $J$ = 8.0 Hz), 1.50 (3H, d, $J$ = 6.4 Hz), 1.96 (1H, d, $J$ = 8.0 Hz), 2.97 (1H, br s), 3.19 (1H, s), 3.28 (1H, q, $J$ = 6.4 Hz), 4.41 (1H, br s), 6.30−6.38 (1H, m), 6.60−6.70 (1H, m), 6.78−6.83 (1H, m), 6.86−6.93 (2H, m), 7.17−7.21 (2H, m), 7.38−7.42 (1H, m), 7.56−7.62 (1H, m), 7.66−7.76 (2H, m) and 7.86−7.94 (2H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 22.0, 44.1, 52.1, 63.4, 63.8, 69.2, 121.3, 125.2, 126.6, 126.7, 127.3, 127.5, 128.1, 128.67, 128.70, 132.5, 134.8, 137.6, 144.5, 147.1 and 164.8; MS (EI) *m*/z (rel intensity) 326 (M$^+$, <1%), 258 (21), 211 (16), 205 (34), 154 (37), 105 (100) and 79 (32). Anal. Calcd for $C_{23}H_{22}N_2$: C, 84.62; H, 6.79; N, 8.58. Found: C, 84.71; H, 6.59; N, 8.70.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(4-quinolyl)hept-5-ene (5e).** Conversion of the aldehyde into the corresponding imine was achieved after stirring overnight at room temperature. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a yellow oil: $[\alpha]^{24}_D$ +85.7 (*c* 1.6, $CH_2Cl_2$); IR ($CH_2Cl_2$, cm$^{-1}$) 2823, 1556, 1408, 1093 and 985; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.38 (1H, d, $J$ = 8.4 Hz), 1.52 (3H, d, $J$ = 6.4 Hz), 1.75 (1H, d, $J$ = 8.4 Hz), 2.79 (1H, br s), 3.24 (1H, q, $J$ = 6.4 Hz), 3.57 (1H, s), 4.40 (1H, br s), 6.36−6.42 (1H, m), 6.74−6.78 (1H, m), 6.82−6.88 (2H, m), 7.12−7.18 (2H, m), 7.40−7.46 (1H, m), 7.54−7.60 (1H, m), 7.78−7.82 (1H, m), 7.82−7.88 (1H, m) and 7.96−8.00 (1H, m); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 21.6, 44.8, 51.1, 63.0, 63.2, 63.7, 121.3, 122.4, 125.7, 126.0, 126.7, 127.5, 128.0, 128.1, 130.0, 133.0, 136.4, 144.0, 147.6, 149.2 and 149.8; MS (EI) *m*/z (rel intensity) 326 (M$^+$, <1%), 242 (18), 226 (11), 176 (49), 106 (37), 105 (100) and 79 (35). Anal. Calcd for $C_{23}H_{22}N_2$: C, 84.62; H, 6.79; N, 8.58. Found: C, 84.67; H, 6.83; N, 8.50.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(2-imidazoyl)hept-5-ene (5g).** Conversion of the aldehyde into the corresponding imine was achieved after stirring overnight at room temperature. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a colorless oil: $[\alpha]^{24}_D$ +154.0 (*c* 1.1, $CH_2Cl_2$); IR (KBr, cm$^{-1}$) 3181, 3027, 1555, 1451 and 1091; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.45 (1H, d, $J$ = 8.4 Hz), 1.47 (3H, d, $J$ = 6.4 Hz), 1.61 (1H, d, $J$ = 8.4 Hz), 3.00 (1H, br s), 3.16 (1H, s), 3.17 (1H, q, $J$ = 6.4 Hz), 4.27 (1H, br s), 6.28−6.33 (1H, m), 6.53−6.55 (1H, m), 6.53−6.55 (1H, bs), 6.78 (1H, bs), 7.09−7.22 (5H, m) and 8.65 (1H, bs); $^{13}$C NMR ($CDCl_3$, 400 MHz) $\delta$ 21.3, 45.7, 50.1, 61.0, 63.7, 63.0, 63.3, 114.0, 127.2, 127.6, 128.1, 132.5, 136.9, 144.9 and 150.5; MS (EI) *m*/z (rel intensity) 283 (M$^+$, <1%), 199 (40), 183 (38), 131 (100), 130 (19), 105 (40), 103 (20) and 77 (17). Anal. Calcd for $C_{17}H_{19}N_3$: C, 76.94; H, 7.22; N, 15.84. Found: C, 77.12; H, 7.09; N, 15.79.

**(1*S*,3*R*,4*R*)-2-[(*S*)-1-Phenylethylamino]azabicyclo[2.2.1]-3-(2-thiazoyl)hept-5-ene (5h).** Conversion of the aldehyde into the corresponding imine was achieved after stirring overnight at room temperature. After reaction of the imine with cyclopentadiene and purification, the cycloaddition product was obtained as a pale yellow oil: $[\alpha]^{24}_D$ +243.0 (*c* 1.1, $CH_2Cl_2$); IR (KBr, cm$^{-1}$) 3446, 2970, 2887, 1455, and 1136; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.44 (1H, d, $J$ = 8.4 Hz), 1.45 (3H, d, $J$ = 6.4 Hz), 1.99 (1H, d, $J$ = 8.4 Hz), 2.94 (1H, br s), 3.24 (1H, q, $J$ = 6.4 Hz), 3.26 (1H, br s), 4.30 (1H, br s), 6.28−6.33 (1H, m), 6.50−6.60 (1H, m), 6.95−6,98 (1H, d, $J$ = 3.2 Hz) and 7.00−7.09 (4H, m), 7.18−7.26 (2H, m) and 7.43 (1H, d $J$ = 3.2 Hz; $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 21.3, 45.2, 51.3, 63.0, 63.3, 64.5, 117.8, 126.8, 127.5, 128.4., 133.0, 136.5, 141.6 and 143.7; MS (EI) *m*/z (rel intensity) 282 (M$^+$, <1%), 201 (26), 183 (89), 132 (13), 131 (100), 130 (31), 105 (56) and 103 (14). Anal. Calcd for $C_{17}H_{18}N_2S$: C, 72.30; H, 6.43; N, 9.92. Found: C, 72.44; H, 6.35; N, 10.16.

**5-Methyl-1-[(*S*)-1-phenylethyl]-1,2,3,6-tetrahydro-[2,3′]-bipyridinyl (6).** The imine was prepared in 1 h from pyridine-3-carboxaldehyde and (*S*)-1-phenylethylamine according to the same procedure described above. To a 40% solution of $ZnCl_2$ (2.2 equiv to the imine) in $CH_2Cl_2$/ether at room temperature and under argon atmosphere was slowly added a solution of the imine in $CH_2Cl_2$, followed by the addition of isoprene (3 equiv to the imine). The resulting mixture was stirred at room temperature for 96 h and then quenched by the addition of saturated $NaHCO_3$ solution. Extraction and solvent evaporation afforded a residue that was purified by flash chromatography (EtOAc/pentane) to give a 4:1 mixture of isomers in 31% yield as pale yellow oil: $[\alpha]^{24}_D$ −49.9 (*c* 1.0, $CH_2Cl_2$); IR (neat, cm$^{-1}$) 2970, 2908, 1449 and 1125; $^1$H NMR ($CDCl_3$, 400 MHz) major isomer $\delta$ 1.28 (3H, d, $J$ = 6.4 Hz), 1.70 (3H, s), 2.26−2.32 (2H, m), 2.75−2.81 (1H, m), 3.07−3.12 (1H, m), 3.77 (1H, q, $J$ = 6.4 Hz) 3.95 (1H, dd, $J$ = 6.4, 5.6 Hz), 5.37 (1H, br s), 7.19−7.40 (6H, m), 7.76−7.79 (1H, m), 8.45−8.53 (1H, m) and 8.66 (1H, d, $J$ = 2.0 Hz); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 12.9, 22.7, 38.0, 43.4, 56.8, 56.9, 119.9, 123.5, 126.6, 126.9, 127.5, 128.1, 128.3, 131.1, 135.4, 148.6, and 149.6, MS (EI) *m*/z (rel intensity) 278 (M$^+$, 24%), 264 (22), 263 (100), 195 (25), 174 (25), 173 (55), 159 (31), 131 (25) and 105 (40). Anal. Calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.90; H, 8.09; N, 10.01.

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