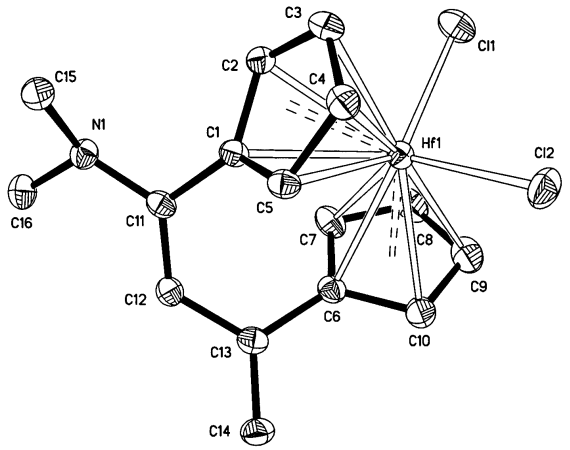


Figure 2. The molecular structure of **4**. Selected bond lengths [Å] and angles [°]: Hf1–C1 2.509(4), Hf1–C2 2.486(4), Hf1–C3 2.495(5), Hf1–C4 2.513(4), Hf1–C5 2.479(4), C1–C11 1.476(6), C11–C12 1.363(6), C12–C13 1.459(6), C6–C13 1.492(6), C13–C14 1.354(6), N1–C11 1.389(6), N1–C16 1.414(7); Cl2-Hf1-Cl1 96.31(5), C1-Hf1-C6 73.77(14), C12-C11-C1 123.0(4), C11-C12-C13 124.6(4), C6-C13-C12 117.9(4), C14-C13-C6 119.4(4).

and 2.163 Å, and the corresponding Cp(centroid)-Zr-Cp′(centroid) angle is 128.4°. The single and double bonds of the bridging allyl group are 1.476(6) and 1.363(6) Å long, respectively, and the N1–C11 bond length is 1.389(6) Å.

*Experimental Section*

**2**: In an typical run a solution of $LiCH(SiMe_3)_2$ (7.4 mmol, 1.23 g) in THF (ca. 10 mL) was added dropwise to a solution of **1** (1 g, 7.4 mmol) in THF (ca. 20 mL) at 0 °C with stirring. The mixture was allowed to warm to room temperature for 2 h. The solvent was removed in vacuo to give **2** as a light brown powder (1.02 g, 98 %). $^1$H NMR (300 MHz, [D$_6$]benzene): $\delta = 6.76$, 6.54 (d, 4H; Cp), 4.48, 4.05 (d, 2H; $CH_2$), 2.94 (*s*, 6H; $NMe_2$).

**3**: $ZrCl_4$ (0.85 g, 3.6 mmol) was added in several portions with stirring to a solution of **2** (1.02 g, 7.2 mmol) in THF (ca. 20 mL) at −78 °C. The mixture was allowed to warm to room temperature and stirred overnight. The solvent was removed in vacuo. The residue was extracted with dichloromethane, and the extract filtered. The solvent was slowly removed from the filtrate in vacuo to give yellow crystalline **3** (1.30 g, 91 % ). Elemental analysis calcd for $C_{16}H_{17}Cl_2NZr$ (385.43): C 49.81, H 4.41, N 3.63; found: C 48.71, H 4.28, N 3.41; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 6.74$, 6.14, 6.08 (m, 8H; Cp), 5.62 (s, 1H; CH), 5.03, 4.93 (d, 2H; $CH_2$), 2.62 (s, 6H; $NMe_2$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 148.7$, 140.2, 138.0, 126.9 (*ipso*-C), 125.0, 124.5, 114.9, 112.0 (CH of Cp), 111.6 ($CH_2$), 105.8 (CH), 42.7 ($NMe_2$).

**4**: The procedure is similar to that of **3**, except that $Et_2O$ was used as the solvent instead of THF. The reaction of $HfCl_4$ (1.20 g, 3.74 mmol) and **2** (1.05 g, 7.44 mmol) resulted in yellow crystalline **4** (1.10 g, 77 % ). Elemental analysis calcd for $C_{16}H_{17}Cl_2NHf$ (472.70): C 40.65, H 3.62, N 2.96; found: C 40.64, H 3.39, N 3.00; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 6.65$, 6.07, 5.99 (m, 8H; Cp), 5.62 (s, 1H; CH), 4.99, 4.95 (d, 2H; $CH_2$), 2.64 (s, 6H; $NMe_2$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 147.3$, 138.8, 134.5, 124.6 (*ipso*-C), 122.1, 121.7, 111.9, 108.9 (CH of Cp), 110.7 ($CH_2$), 104.3 (CH), 41.4 ($NMe_2$).

Crystal data for **3**: $C_{16}H_{17}Cl_2NZr$, $M_r = 385.43$, monoclinic, space group $P2_1/n$, $a = 10.8208(9)$, $b = 10.5382(12)$, $c = 13.9891(10)$ Å, $\beta = 101.380(5)°$, $V = 1563.8(2)$ Å$^3$, $F(000) = 776$; $Z = 4$, $\rho_{calcd} = 1.637$ g cm$^{-3}$, $\mu(Mo_{K\alpha}) = 10.33$ cm$^{-1}$, $T = 294(2)$ K, crystal size $0.38 \times 0.36 \times 0.08$ mm, 3504 unique reflections for $2.18 < \theta < 25.00°$, 2722 reflections with $I > 2\sigma(I)$; $R = 0.0269$, $R' = 0.0380$, $S = 0.917$.

Crystal data for **4**: $C_{16}H_{17}Cl_2NHf$, $M_r = 472.70$, monoclinic, space group $P2_1/n$, $a = 10.830(2)$, $b = 10.516(2)$, $c = 13.965(3)$ Å, $\beta = 101.51(3)°$, $V = 1558.5(2)$ Å$^3$, $F(000) = 904$; $Z = 4$, $\rho_{calcd} = 2.015$ g cm$^{-3}$, $\mu(Mo_{K\alpha}) = 10.33$ cm$^{-1}$, $T = 294(2)$ K, crystal size $0.40 \times 0.38 \times 0.20$ mm, 2827 unique reflections for $2.18 < \theta < 25.55°$, 2813 reflections with $I > 2\sigma(I)$; $R = 0.0446$, $R' = 0.0482$, $S = 0.933$.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-114199 (**3**) and CCDC 114200 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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# A Convenient and Versatile Route to Hydroquinolines by Inter- and Intramolecular Aza-Diels – Alder Pathways**

Henning Steinhagen and E. J. Corey*

Described herein is a practical method for the generation of *o*-azaxylylenes and their application to the synthesis of a variety of hydroquinoline derivatives. The formation of *o*-azaxylylenes has previously been reported by photochemical fragmentation,[1, 2] fluoride induced elimination of *o*-trime-

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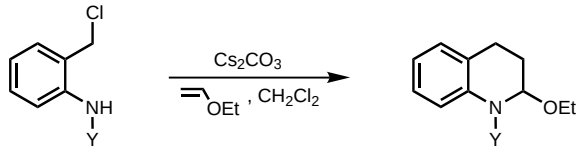
thylsilylaminobenzyltrimethylammonium salts,[3] and by pyrolytic elimination of *o*-hydroxymethylanilines at 140–180 °C.[4] Surprisingly, the simplest method possible for *o*-azaxylylene production, base-induced elimination of hydrogen chloride from amide or sulfonamide derivatives of *o*-chloromethylaniline, has never been reported. We have found that this process is highly effective for the generation of *o*-azaxylylenes and that these intermediates are readily trapped by olefins, especially π-electron-rich olefins, to form hydroquinoline derivatives as exemplified in Scheme 1.[5] The



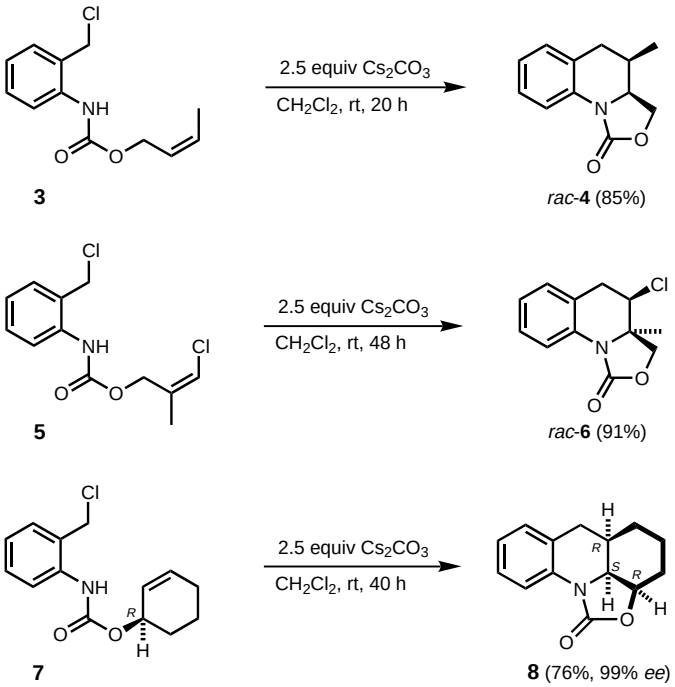

**1a**, Y = $SO_2Me$
**1b**, Y = $SO_2p$Tol
**1c**, Y = $CO_2t$Bu

**2a**, Y = $SO_2Me$ (78%)
**2b**, Y = $SO_2p$Tol (74%)
**2c**, Y = $CO_2t$ Bu (83%)

Scheme 1. Generation and trapping by ethyl vinyl ether of *o*-azaxylylenes.

synthesis of hydroquinolines **2a** and **2b** was conducted at −78 °C with addition of the chloromethylaniline derivative to the reaction mixture containing ethyl vinyl ether (2 equiv) and cesium carbonate (2.5 equiv) in dichloromethane over 4 h by syringe pump.[6] The hydroquinoline **2c** was prepared in a similar manner but with addition by syringe pump at 23 °C over 24 h.

This new approach to hydroquinolines is especially powerful in the intramolecular version. As shown in Scheme 2, these intramolecular reactions proceed under mild conditions and provide hydroquinolines **4**, **6**, and **8** stereospecifically by a




Scheme 2. Intramolecular [2+4] cycloaddition reactions of *o*-azaxylylenes to form tri- and tetracyclic hydroquinolines.

suprafacial (*cis*) cycloaddition. The structures of the products were unambiguously determined in each case by X-ray crystallographic analysis.[7] In each case NMR analysis of the crude reaction mixture indicated the absence of diastereomeric product.

The formation of the 3-chlorotetrahydroquinoline derivative **6** is especially interesting because this structure represents the core of the potent antiviral agent virantmycin,[8] previously accessible only by lengthy multistep routes.[9] The enantiospecific synthesis of the chiral tetracyclic tetrahydroquinoline **8** ($[\alpha]_D^{25} = +82$, $c = 0.95$ in $CHCl_3$, 99 % *ee* by chiral HPLC analysis)[10] from the readily available precursor **7**[11] is also noteworthy and illustrative of the potential of this method for the production of enantiomerically pure (≥ 99 % *ee*) products. X-ray crystallographic analysis of **8** provided proof of the stereochemistry and demonstrated a molecular conformation in which the chair-form cyclohexane ring is approximately orthogonal to the planar tricyclic core (Figure 1).

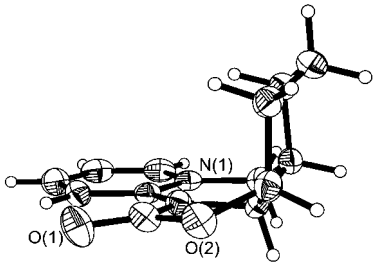
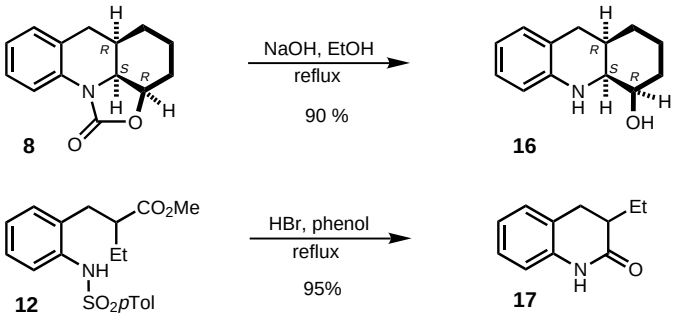



Figure 1. ORTEP plot of **8** as determined by X-ray crystallography.[7c]

A variety of other trapping experiments with in situ generated *o*-azaxylylenes are summarized in Table 1. Vinyl ether substrates generally gave the products of [2 + 4] cycloaddition (**9**, **10**, **11**). On the other hand, ketene acetals afforded the conjugate adduct (**12** with **1b**) and the cycloadduct (**13** with **1c**). The π-electron-rich substituted acetylenes *N*,*N*-diethyl-1-propynylamine and 1-ethoxy-1-propyne furnished the dihydroquinoline derivatives **14** and **15**. In contrast, the π-electron-deficient dienophile ethylpropiolate did not afford Diels–Alder products with the *o*-azaxylylenes from **1b** or **1c**.




The various products described above can be transformed into a variety of compounds. For example, the tetracyclic carbamate **8** is easily cleaved upon treatment with ethanolic NaOH to the corresponding chiral tricyclic aminoalcohol **16**

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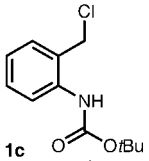
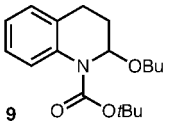
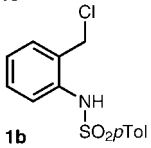
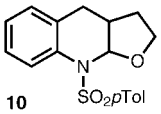
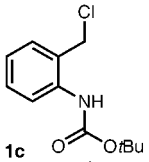
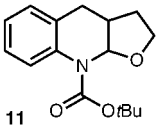
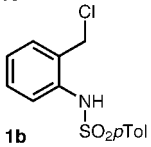
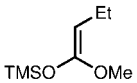
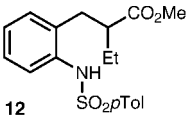
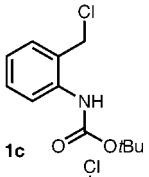
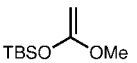
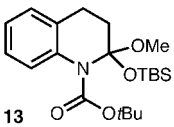
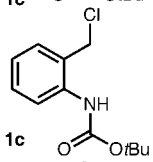
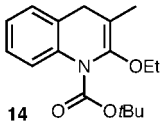
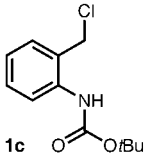
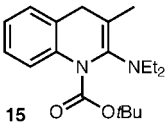
Table 1. Trapping reactions of *o*-azaxylylenes with π-electron-rich dienophiles.

| Substrate | Dienophile | Conditions[a] | Product | Yield [%][b] |
|---|---|---|---|---|
|  **1c** |  | **C** |  **9** | 95 |
|  **1b** |  | **A** |  **10** | 91 |
|  **1c** |  | **B** |  **11** | 90 |
|  **1b** |  | **A** |  **12** | 90 |
|  **1c** |  | **B** |  **13** | 40 |
|  **1c** |  | **B** |  **14** | 60 |
|  **1c** |  | **B** |  **15** | 95 |

[a] **A**: 2 h, −78 °C, 10 equiv dienophile, addition of substrate over 15 min; **B**: 24–48 h, rt, 10 equiv dienophile, addition of substrate over 1 min; **C**: 24 h, rt, 2 equiv dienophile, addition of substrate by syringe pump over 24 h; [b] yields of isolated products after chromatography on silica gel with mixtures of hexane/EtOAc (+1% $NEt_3$ for **14** and **15**) for elution.

($[\alpha]_D^{25} = +53$, $c = 0.9$ in $CHCl_3$), and the sulfonamide **12** underwent cyclization with HBr/phenol to the bicyclic lactam **17** in 95% yield.

The reactions described herein define a practical and versatile method for the generation and use of *o*-azaxylylenes in aza-Diels–Alder reactions which proceed from readily available precursors and under mild conditions.

## *Experimental Section*

All reactions were carried out under an inert atmosphere with anhydrous solvents.

**7**: A solution of (*R*)-2-cyclohexen-1-ol[10] (147 mg, 1.5 mmol) in diethyl ether (1 mL) was added to a solution of phosgene (3 mmol) in toluene (1.6 mL) at −78 °C. The mixture was stirred at −15 °C for 3 h and at 0 °C for an additional 30 min. This solution of chloroformate was transferred by cannula to a solution of *o*-aminobenzyl alcohol (Alfa, 185 mg, 1.5 mmol) and pyridine (0.14 mL, 1.7 mmol) in dichloromethane (5 mL) over 15 min at 0 °C. The reaction mixture was warmed to 23 °C and stirred for an additional 2 h. Aqueous workup and chromatography on silica gel with hexane/ethyl acetate (6/1) afforded the hydroxy carbamate coupling product as a colorless crystalline solid (282 mg, 76%). M.p. 91–92 °C; $[\alpha]_D^{25} = +150$ ($c =$ 0.77 in $CHCl_3$); IR (film): $\tilde{\nu} = 3348, 3344, 2939, 1731, 1702, 1593, 1529, 1454, 1305, 1231, 1219, 1192, 1040, 1008, 938\ cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.94$ (d, $J = 8$ Hz, 1H), 7.82 (br s, 1H, NH), 7.32 (t, $J = 7.4$ Hz, 1H), 7.17 (d, $J = 7.4$ Hz, 1H), 7.03 (t, $J = 7.4$ Hz, 1H), 5.95–6.00 (m, 1H), 5.78–5.83 (m, 1H), 5.26–5.29 (m, 1H), 4.69 (d, $J = 5.2$ Hz, 2H), 2.16 (t, $J = 5.6$ Hz, 1H, OH), 1.60–2.14 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 153.98$, 137.82, 132.70, 129.25, 129.00, 128.96, 126.00, 123.38, 121.12, 69.04, 64.28, 28.57, 24.94, 18.94; HR-MS (EI): calcd (found) for $C_{14}H_{17}NO_3$ [$M^+$]: 247.1208 (247.1218). A solution of thionyl chloride (102 μL, 1.40 mmol) in dichloromethane (4 mL) was added over 15 min to a solution containing the hydroxy carbamate (240 mg, 0.97 mmol) and triethylamine (195 μL, 1.40 mmol) in dichloromethane (4 mL). The solution was stirred for 2 h and the solvent was removed in vacuo. Chromatography of the crude product on silica gel with hexane/ethyl acetate (6/1) afforded **7** as a colorless crystalline solid (230 mg, 89%). M.p. 120–121 °C; $[\alpha]_D^{25} = +141$ ($c = 0.95$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3285, 3037, 3029, 2945, 2913, 1687, 1590, 1527, 1456, 1296, 1248, 1049\ cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 7.87$ (d, $J = 7.8$ Hz, 1H), 7.37 (t, $J = 1.4$, 7.8 Hz, 1H), 7.28 (d, $J = 1.4$, 7.6 Hz, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 6.87 (br s, 1H, NH), 5.98–6.02 (m, 1H), 5.79–5.83 (m, 1H), 5.29–5.31 (m, 1H), 4.62 (s, 2H), 1.65–2.14 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 153.66$, 136.89, 132.94, 130.14, 130.08, 127.19, 125.83, 124.30, 122.82, 69.40, 44.03, 28.56, 24.94, 18.92; HR-MS (EI): calcd (found) for $C_{14}H_{16}NO_2Cl$ [$M^+$]: 265.0869 (265.0878).

**8**: A suspension of **7** (53 mg, 0.2 mmol) and cesium carbonate (163 mg, 0.5 mmol) in dichloromethane (5 mL) was stirred for 40 h at 23 °C. The reaction mixture was filtered through a pad of celite and the solvent was evaporated in vacuo. Chromatography of the crude product on silica gel with hexane/ethyl acetate (6/1) gave **8** as a colorless crystalline solid (35 mg, 76%). M.p. 149–150 °C; $[\alpha]_D^{25} = +82$ ($c = 0.95$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2929, 1744, 1494, 1459, 1390, 1364, 1349, 1339, 1324, 1293, 1227, 1209, 1185, 1135, 1104, 1060, 994, 946\ cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 8.40$ (d, $J = 8.4$ Hz, 1H), 7.21 (t, $J =$ 7.8 Hz, 1H), 7.10 (d, $J = 7.5$ Hz, 1H), 6.98 (t, $J = 7.4$ Hz, 1H), 4.64 (dt, $J = 6.6$, 8.6 Hz, 1H), 4.26 (dd, $J = 3.8$, 6.6 Hz, 1H), 3.12 (dd, $J = 5.9$, 16.7 Hz, 1H), 2.65 (d, $J = 16.4$ Hz, 1H), 2.08–2.22 (m, 2H), 1.71–1.77 (m, 1H), 1.44–1.61 (m, 2H), 1.31–1.36 (m, 1H), 1.15–1.22 (m, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 154.28, 134.50, 129.47, 127.06, 122.74, 122.09, 116.31, 73.06, 56.03, 32.55, 29.19, 27.14, 24.44, 19.66$; HR-MS (FAB): calcd (found) for $C_{14}H_{15}NO_2Na$ [$M + Na^+$]: 252.1000 (252.1008).

**16**: A solution of **8** (31.5 mg, 0.137 mmol) in 10% ethanolic NaOH (2 mL) was heated at reflux for 1 h. After evaporation of the solvent in vacuo the mixture was suspended in water (5 mL) and extracted with chloroform (10 mL × 3). The combined organic layers were dried over sodium sulfate, filtered, and the solvent was removed in vacuo. Chromatography of the crude mixture on silica gel with hexane/ethyl acetate (6/1) afforded the chiral aminoalcohol **16** as a colorless crystalline solid (25 mg, 90%). M.p. 134–135 °C; $[\alpha]_D^{25} = +53$ ($c = 0.9$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3419, 3405, 3378, 3371, 3300, 3235, 3225, 3201, 3017, 2936, 2920, 2895, 2855, 1606, 1504, 1496, 1486, 1444, 1374, 1289, 1104, 1054, 1043, 1008\ cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 6.97$ (t, $J = 7.6$ Hz, 1H), 6.93 (d, $J = 7.4$ Hz, 1H), 6.57 (t, $J = 7.3$ Hz, 1H), 6.49 (d, $J = 8$ Hz, 1H), 4.21 (br s, 1H, NH), 3.81–3.85 (m, 1H), 3.64 (t, $J = 3$ Hz, 1H), 3.03 (dd, $J = 5.6$, 16.2 Hz, 1H),

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2.50 (dd, $J = 1.6$, 16.2 Hz, 1H), 1.89–1.93 (m, 1H), 1.73–1.81 (m, 2H), 1.60–1.63 (m, 1H), 1.55 (brs, 1H, OH), 1.28–1.40 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 143.47$, 129.73, 126.68, 119.18, 116.49, 113.43, 72.67, 53.93, 33.16, 32.96, 27.80, 25.31, 23.35; HR-MS (CI): calcd (found) for $C_{13}H_{17}NO$ [$M^+$]: 204.1388 (204.1397).

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[6] The substrates **1a**–**1c** of Scheme 1 were prepared from *o*-aminobenzyl alcohol by the sequence: 1) *N*-acylation or *N*-sulfonylation, and 2) conversion of the resulting benzyl alcohol into the corresponding chloride by reaction with thionyl chloride in dichloromethane.
[7] a) Crystal structure data for **4**: $C_{12}H_{13}NO_2$; monoclinic; $P2_1c$; $a = 14.972(7)$, $b = 5.599(3)$, $c = 13.403(5)$ Å; $\alpha = 90$, $\beta = 114.93(3)$, $\gamma = 90°$; $Z = 4$; $R_1$ [$I > 2\sigma(I)$] = 0.0386; b) crystal structure data for **8**: $C_{14}H_{15}NO_2$; monoclinic; $P2_1c$; $a = 17.7653(11)$, $b = 9.1414(6)$, $c = 15.4356(10)$ Å; $\alpha = 90$, $\beta = 115.5670(10)$, $\gamma = 90°$; $Z = 8$; $R_1$ [$I > 2\sigma(I)$] = 0.0481; c) crystal structure data for **6**: $C_{12}H_{12}NO_2Cl$; monoclinic; $P2_1n$; $a = 6.2128(5)$, $b = 12.1974(12)$, $c = 14.4788(13)$ Å; $\alpha = 90$, $\beta = 98.188(3)$, $\gamma = 90°$; $Z = 4$; $R_1$ [$I > 2\sigma(I)$] = 0.0601. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-113239/113240/113241. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
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[10] Chiralpak AD column (Daicel Chemical Industries); flow rate: 0.7 mL min$^{-1}$; eluent: 6% *i*PrOH in hexane; UV detection at 254 nm; $t_R$[(+)-**8**] = 26.4 min, $t_R$[(−)-**8**] = 30.0 min.
[11] The substrates **3**, **5**, and **7** were prepared starting from the corresponding allylic alcohols by the sequence: 1) conversion into chloroformates by reaction with phosgene, 2) treatment of the chloroformates with *o*-aminobenzyl alcohol, and 3) conversion of the resulting hydroxy carbamates into the corresponding chlorides with thionyl chloride (see experimental section for details). 3-Chloro-2-methyl-2-propen-1-ol was prepared according to A. Mooradian, J. B. Cloke, *J. Am. Chem. Soc.* **1946**, *68*, 785–789; L. F. Hatch, J. J. Russ, L. B. Gordon, *J. Am. Chem. Soc.* **1947**, *69*, 2614–2616. Enantiomerically pure (*R*)-2-cyclohexen-1-ol was prepared by kinetic resolution with lipase as described by T. Fukazawa, T. Hashimoto, *Tetrahedron: Asymmetry* **1993**, *4*, 2323–2326.

# *re*- and *si*-Face-Selective Nitroaldol Reactions Catalyzed by a Rigid Chiral Quaternary Ammonium Salt: A Highly Stereoselective Synthesis of the HIV Protease Inhibitor Amprenavir (Vertex 478)**

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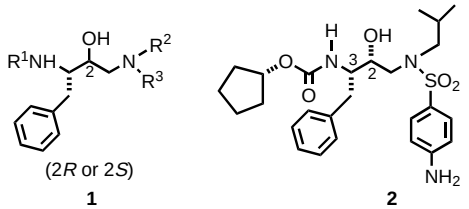
The development of therapeutically useful HIV protease inhibitors has been one of the major contributions of synthetic and medicinal chemistry to human well-being during this decade.[1, 2] Since several of these agents possess chiral substituted 1,3-diamino-2-hydroxypropyl segments as a central structural subunit, for example, the phenylalanine-related subunit **1**, considerable research effort has been directed at methods for their synthesis.[3, 4] Described herein is a new strategy for stereocontrol in the synthesis of subunits of type **1** and a specific application with a practical synthesis of amprenavir (**2**),[5, 6] an important second generation HIV




protease inhibitor with a number of clinical advantages over first generation agents. The method currently being used to produce **2** involves the activation of the carboxyl group of *N*-*tert*-butoxycarbonylphenylalanine and transformation to the corresponding diazomethyl ketone with diazomethane as a key element.[7] Because of the intrinsic hazards of this step a safer alternative seems preferable.

The sequence utilized for the synthesis of amprenavir is summarized in Scheme 1. *N*,*N*-Dibenzyl-(*S*)-phenylalaninal (**3**)[8] in tetrahydrofuran (THF) was added to a mixture of quaternary ammonium salt **4**,[9, 10] nitromethane, and finely divided potassium fluoride in THF with stirring. After 6 h the nitro alcohol **5** was isolated in 86% yield by flash chromatography on silica gel.[10] The more polar C(2) diastereomer of **5** was isolated in 5% yield, which indicated a 17:1 diastereoselectivity for the nitroaldol reaction.[11] In contrast, the nitroaldol reaction of **3** in the presence of tetra-*n*-butylammonium fluoride[8c] afforded a mixture of **5** and the C(2) diastereomer with only 4:1 diastereoselectivity under the same reaction conditions. Treatment of nitro alcohol **5** with 2.5 equivalents of $NiCl_2$ and 25 equivalents of $NaBH_4$ in methanol at 0 °C for 10 min with vigorous agitation provided

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