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A scalable and expedient method of preparing diastereomerically and enantiomerically enriched pseudonorephedrine from norephedrine☆

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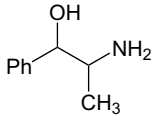
Abstract—Norephedrine has been efficiently converted into the corresponding diastereomer pseudonorephedrine using a three step, one-pot reaction. The three step process involves treatment of norephedrine with di-*tert*-butyl dicarbonate (Boc_2O); cyclization by way of mesylate formation at the alcohol; and lithium hydroxide mediated hydrolysis of the oxazolidinone. The diastereomeric purity was determined by HPLC and the enantiomeric purity was determined by optical activity measurements and chiral stationary phase HPLC analysis of the pseudonorephedrine oxazolidinone derivatives.

1. Introduction

The *Ephedra* alkaloids, norephedrine[1] and pseudoephedrine[2] have proven to be very useful starting materials in the preparation of chiral auxiliaries for stoichiometric applications,[1a–g,2a–e] and for the preparation of chiral ligands for catalytic asymmetric synthesis.[1h–l,2f–j] Our research group has recently become interested in the development of chiral ligands based on the corresponding diastereomer of norephedrine, namely pseudonorephedrine (Fig. 1). Pseudonorephedrine is also known as either norpseudoephedrine or cathine. The availability of pseudonorephedrine from commercial sources is apparently limited as it is a component from the extraction of the khat shrub (*Catha edulis*) found in eastern Africa (e.g., Ethiopia) and Saudi Arabia.[3]



(1*S*,2*S*)-pseudonorephedrine **1a**
(1*R*,2*R*)-pseudonorephedrine **1b**
(1*R*,2*S*)-norephedrine **2a**
(1*S*,2*R*)-norephedrine **2b**

Figure 1. Pseudonorephedrines **1a** and **b** and norephedrines **2a** and **b**.

The asymmetric synthesis of pseudonorephedrine has been accomplished with varying degrees of success using a wide range of methods. Most of these reported methods afford moderate diastereoselectivities at best and often require the use of chromatography, relatively expensive reagents, halogenated solvents, and excessive amounts of time. Many of the reported methods with higher diastereoselectivities lack the scalability to produce pseudonorephedrine on a useful academic or commercial level.

A previous report of a 'convenient' synthesis of pseudonorephedrine involved an intermediate taken from the synthesis of chloramphenicol.[4a] Through a sequence of seven reactions, this process afforded pseudonorephedrine in an overall yield of 26%. The authors report a specific rotation value suggesting a high enantiomeric purity,[4b] but do not address the enantiomeric ratio in a more rigorous fashion. Lee et al. also prepared pseudonorephedrine by reaction of organometallic reagents with enantiomerically enriched aziridine-2-carboxaldehydes. The diastereomeric ratios obtained ranged from 91:9 to 94:6 and required flash chromatography to further enhance them.[5] In addition to these methods, Claremon et al. carried out the addition of methyllithium to a chiral, non-racemic α-substituted hydrazone to prepare pseudonorephedrine.[6] However, this method

☆ A patent application has been filed.

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involved multiple steps as well as a kinetic resolution protocol to generate the key starting material.[7] Cho et al. carried out the reduction of racemic β-propiophenones by using a double asymmetric induction protocol that involved a partial kinetic resolution.[8] This method afforded diastereomeric ratios that strongly favored the formation of norephedrine over pseudonorephedrine. Reddy et al. prepared the related pseudoephedrine in a series of steps including the reaction of an L-alanine derived oxazolidine with phenylmagnesium bromide to afford an inseparable mixture of diastereomers (95:5) favoring the pseudoephedrine related diastereomer.[9]

There have been other studies conducted that have afforded moderate to good diastereoselectivities. Moran et al.[10] have prepared pseudonorephedrine by employing an enzymatic reduction of an α-keto-*O*-methyloxime that required 30 g of Baker's yeast and 30 g of sucrose to convert 0.53 g of substrate into 0.28 g of product. The diastereoselective reduction of the resultant α-hydroxy-*O*-methyloxime product with lithium aluminum hydride afforded pseudonorephedrine with a diastereoselectivity of 4:1.[10]

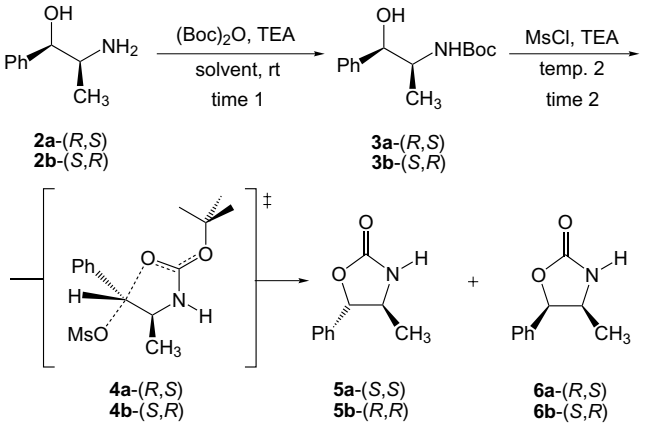
Agami et al.[11a] prepared a pseudonorephedrine based oxazolidinone using a technique that involved the formation and isolation of *N*-*tert*-butoxycarbonylnorephedrine.[11b,c] This material was reacted with *p*-toluenesulfonyl chloride to yield the corresponding *O*-tosylnorephedrine derivative, which presumably underwent cyclization to give the oxazolidinone in a highly stereoselective fashion.[11] Davies and Doisneau also obtained the oxazolidinone of pseudonorephedrine by the *n*-BuLi induced epimerization of the C_5-phenyl position of a norephedrine derived oxazolidinone.[12]

Enantiomerically enriched (*S*,*S*)-pseudonorephedrine **1a** from natural sources is available in the United States at an estimated cost of $16,800/g.[13a] Enantiomer **1b** is not readily available for purchase from commercial sources,[13b] due to the fact that it is a minor *Ephedra* alkaloid in the *C. edulis* plant.[14] It is probable that the relative expense and lack of an efficient synthetic process have hindered research concerning the uses and effects of pseudonorephedrine. In conjunction with our interest in developing structurally novel catalytic systems, we sought to develop a process that would afford either enantiomer of pseudonorephedrine with minimal time and expense, while simultaneously affording high diastereoselectivity and enantiomeric purity. Herein, we report a new process that allows the formation of enantiomerically enriched pseudonorephedrine from norephedrine in high diastereomeric purity and good overall yield in a process that is inexpensive, expedient, and scalable.

2. Results and discussion

The initial process that was pursued involved formation of the pseudonorephedrine based oxazolidinone from norephedrine from a one-pot reaction. To this end, norephedrines **2a** and **2b** were reacted with di-*tert*-butyl dicarbonate and triethylamine to afford amide derivatives **3a** and **3b** (Table 1).[15] TLC analysis suggested that the transformation was complete within 2 h. At this point, methanesulfonyl chloride and an additional equivalent of triethylamine were added. This gave rise to the target pseudonorephedrine based oxazolidinones **5a** and **5b**. The putative intermediates **4a** and **4b** were not observed by TLC analysis or by ^{1}H NMR spectroscopy, suggesting that rapid displacement of the mesylate had occurred.[11] This process led to stereochemical inversion of the carbon bearing the phenyl substituent leading to **5a** and **5b** in diastereomeric ratios of ⩾95:5 as determined by HPLC analysis.[16] It is believed that oxazolidinones **6a** and **6b** form as the result of an S_N1 type displacement.

Table 1. Synthesis of the pseudonorephedrine based oxazolidinone



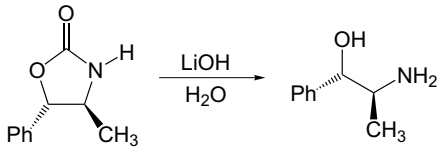
Entry	Solvent	Time 1 (h)	Time 2 (h)	Temp 2[a]	Yield (%)	dr (**5**:**6**)[b]
1	CH_2Cl_2	2	3	40	82	n/a
2	CH_2Cl_2	2	2	40	55	95:5[c]
3	CH_2Cl_2	2	16	25	70	95:5[c]
4	THF	2	2.5	47	89	97:3[c]
5	THF	2	3	49	90	99:1[d]
6	THF	2	3	48	84	99:1[d]

Only the (1*R*,2*S*)-norephedrine pathway is shown.
[a] Temperatures are in degree Celsius (°C).
[b] HPLC data were gathered on a Shimadzu SCL-10 AVP system (dr are reported as *anti*:*syn*).
[c] Crude dr determined by HPLC on a Dynamax-100 Å column.
[d] Crude dr determined by chiral HPLC on a Chiracel-OD column.

Table 1 illustrates the reaction conditions, diastereoselectivities, and yields that were obtained over the course of our optimization studies. The formation of **5a** was accomplished in both dichloromethane and THF solvent systems in good yield, as well as high diastereoselectivity. The most significant difference involved the cyclization process. If the synthesis was carried out in THF, the cyclization process required heating between 45 and 50 °C for 3 h. In contrast, the reaction conducted in methylene chloride underwent cyclization at reflux temperature and required 2–3 h. It was also determined that the reaction in methylene chloride underwent cyclization at room temperature in 16 h. Both processes afforded minimal diastereomeric scrambling in the formation of desired pseudonorephedrine oxazolidinone and the product could be easily purified by trituration with ethyl acetate. It should be noted that cyclization attempts with norephedrine and either *p*-toluenesulfonyl

chloride or triflic anhydride were unsuccessful in both THF and methylene chloride. We also pursued the use of methyl chloroformate at the acylation stage and this process was successful. However, the cyclization failed to progress in a timely manner. The two reaction, one-pot, process involving the Boc-protected norephedrine and cyclization with methanesulfonyl chloride proved to be the best method. The ultimate formation of pseudonorephedrine was completed through the hydrolysis of **5a** and **5b**, which was accomplished in a $LiOH/H_2O$ solution and heating (Table 2).[17] Attempts at hydrolysis with Cs_2CO_3 and K_2CO_3 proved not to be very successful.[18] The stereochemical integrity of the pseudonorephedrine from hydrolysis mixture was determined by ^1H NMR spectroscopy and HPLC. In all cases, the stereochemical purity was directly comparable to the enantiomeric and diastereomeric purity of the starting oxazolidinone. The relative stereochemistry of the product of the hydrolysis was confirmed by X-ray crystallographic analysis (Fig. 2).

Table 2. Hydrolysis of oxazolidinone



5a-(*S*,*S*) **1a**-(*S*,*S*)

Entry	Base %	Time (min)	Temp[a]	Yield (%)
1	10	30	80	82
2	10	45	90	91
3	5	30	85	94

[a] Temperatures are in degree Celsius.

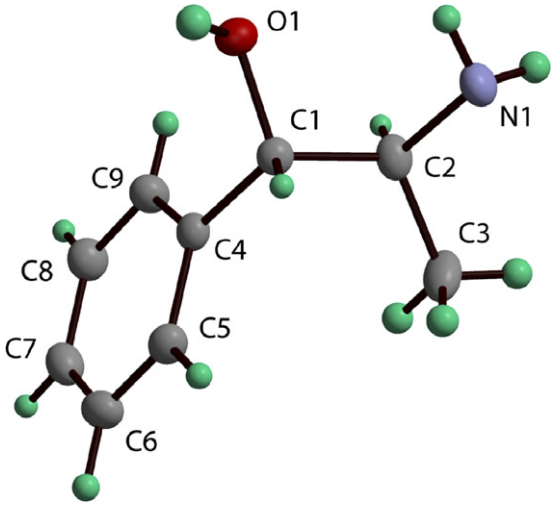
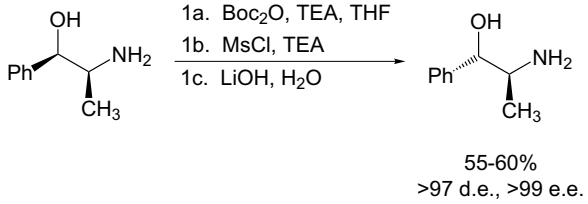


Figure 2. RASTEP drawing of (1*S*,2*S*)-pseudonorephedrine **1a** X-ray crystal structure.

It was at this time that we attempted to combine the cyclization reaction and hydrolysis reaction into a one-pot process to afford pseudonorephedrine (Scheme 1). The solvent



Scheme 1. One-pot synthesis of pseudonorephedrine.

chosen for the one-pot synthesis was THF as chromatographic and ^1H NMR spectroscopic analysis of the two oxazolidinone syntheses indicated that the THF reaction had fewer impurities. In addition, the miscibility of THF and water rendered THF far less troublesome than methylene chloride. The cyclization of the norephedrine to form the pseudonorephedrine oxazolidinone proceeded as expected. The success of the conversion of norephedrine to pseudonorephedrine relied primarily on the lithium hydroxide mediated hydrolysis of the oxazolidinone, which involved temperatures of 80 °C and higher. This required the THF to be removed in order for the thermal requirement to be met. It was determined that the most efficient way to remove THF was through the removal of the solvent under aspirator vacuum, while the reaction vessel was held at a temperature of 60 °C.

Once the THF was removed, the reaction was heated between 85 and 90 °C to induce the hydrolysis process. The extraction process that was developed for this reaction involved initial acidification to remove any impurities such as unreacted oxazolidinone. This allowed the pseudonorephedrine to be efficiently isolated from the extraction and readily purified by a simple trituration process. The diastereoselectivity was not compromised through this one-pot synthesis and the results were comparable as if each of the three reactions had been performed alone. The one-pot synthesis yielded between 55% and 60% of the product, thus suggesting an average yield of 80–85% for each of the three steps.

3. Conclusions

The one-pot synthesis of either enantiomer of pseudonorephedrine in high diastereoselectivity and good yield developed in this work is superior to methods that have been described in the chemical literature. Based on our estimation, the cost of producing either enantiomer from norephedrine is under $10/g, significantly less expensive than the commercially available (1*S*,2*S*)-pseudonorephedrine.[13a] This process also allows for the production of (1*R*,2*R*)-pseudonorephedrine,[13b] which is not readily available through commercial sources. The reagents used in this process are easily available and inexpensive. Relative to other β-aminoalcohols that are used regularly, such as L-phenylalaninol ($19.76/g), L-alaninol ($21.08/g), L-valinol ($14.56/g), L-phenylglycinol ($18.96/g), L-leucinol ($12.52/g) and L-*tert*-leucinol ($58.20/g), pseudonorephedrine is now potentially less expensive than these commonly used substrates.[19] This method now provides a scalable process to

generate these alkaloids in an inexpensive and time efficient process on either an academic or potentially industrial scale.

4. Experimental

4.1. General information

(1*S*,2*R*)-Norephedrine (98% ee) and (1*R*,2*S*)-norephedrine (99% ee) were purchased from Sigma–Aldrich. All reaction vessels were flame dried and purged under a nitrogen atmosphere. Tetrahydrofuran was distilled over lithium aluminum hydride and stored over 4 Å molecular sieves. Triethylamine was distilled over calcium hydride. All extractions were dried over anhydrous magnesium sulfate, gravity filtered, and the solvents removed via rotary evaporation. Infrared data were acquired using a PerkinElmer Spectrum BX FT-IR spectrophotomer on NaCl plates and reported in reciprocal centimeters (cm^{-1}). A Varian FT NMR spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C $\{^{1}H\}$ NMR with all spectra recorded in $CDCl_3$ and reported in parts per million (δ scale) with tetramethylsilane as an internal standard ($\delta = 0.00$ ppm ^{1}H, 77.0 ppm ^{13}C) was used for ^{1}H and ^{13}C spectroscopies. HPLC information was gathered on a Shimadzu HPLC SCL-10AVP instrument with a UV–vis detector operating at 254 nm on either a Dynamax-100 Å (R008010C5) column or a Chiracel-OD (OD00CE-IE048) chiral column, each with a flow rate of 1 mL/min. Optical rotation data were collected on a JASCO P-1010 digital polarimeter operating at 589 nm in a 100 mm cell. Melting points were determined using a Laboratory Devices Mel-Temp apparatus and are uncorrected.

4.2. General procedure for one-pot synthesis of pseudonorephedrine

THF was distilled directly into a 2 L three-neck reaction vessel fitted with an addition funnel and thermometer through a Claisen adapter. To this was added norephedrine to provide a 0.3 M solution. Triethylamine (1.1 equiv) was added via syringe through the Claisen adapter septum to the solution and the vessel was immersed in an ice bath. To this solution was added di-*tert*-butyl dicarbonate (1.05 equiv) and the ice was removed after 5 min. The reaction was allowed to proceed at ambient temperature for 2 h when the reaction was cooled to 0 °C in an ice bath. An additional portion of TEA (1.1 equiv) was added and then methanesulfonyl chloride (1.1 equiv) was added dropwise through the addition funnel. The ice was removed after 5 min and the solution was heated to 48 °C for 3 h to afford a light orange solution. An aqueous 10% LiOH solution equal to the original volume of THF was prepared and added to the solution. The flask was fitted with a distillation arm, condenser, vacuum adapter, and a collection flask with the entire apparatus sealed with vacuum grease. The collection flask was immersed in an ice/NaCl water bath. The main reactor was immersed in a 60 °C water bath. A gentle vacuum was applied by a water aspirator for 45 min until the solvent was removed, after which the vacuum apparatus and the water bath were removed and the heating mantle was replaced under the main vessel (a nearly quantitative recovery of the THF and TEA was achieved). The reaction was then heated to 85–90 °C. The reaction was allowed to proceed in open air with no condenser for one h after which time the heat was removed and the solution was allowed to cool. After the reaction had cooled, the water was acidified with 6 M HCl until the solution turned clear. The pH tested and adjusted with 6 M NaOH to afford an approximate pH of 3–4. Extraction was performed by exposure of the water to chloroform (4×100 mL). The water was then basified with 6 M NaOH until the pH was approximately 8. The water was removed by evaporation until the saturation point was reached (approximately 25% original volume) and the pH was tested and adjusted to afford a pH $\approx$ 8. The water was then exposed to ethyl acetate (6×200 mL), and the solvents dried and removed. The resulting white solid was formed and purification was performed by trituration with diethyl ether, however, the initial washes with chloroform at pH 3–4 removed most impurities. Progress of the reaction was monitored by TLC (1:1 ethyl acetate–hexanes) with the Boc-(1*R*,2*S*)-norephedrine **3** at $R_f \approx 0.64$ and the oxazolidinone (**5**) at $R_f \approx 0.25$.

4.2.1. (1*S*,2*S*)-2-Amino-1-phenyl-1-propanol 1a. White granular crystals (12.02 g) were produced from 20 g of (1*R*,2*S*)-norephedrine (60%). ^{1}H NMR ($CDCl_3$): δ 0.96 (d, 3H, $J = 6.64$ Hz), 2.33 (s, 1H), 2.97 (quintet, 1H, $J = 6.45$ Hz), 4.18 (d, 1H, $J = 7.03$ Hz), 7.25–7.23 (m, 5H). ^{13}C $\{^{1}H\}$ NMR ($CDCl_3$): δ 20.2, 52.9, 78.6, 126.5, 127.4, 128.2, 142.7. FT-IR (Nujol): 1456, 1047, 752, 693. Mp = 72–74 °C. $[\alpha]_D^{28} = +31.8$ (*c* 3.49, EtOH), lit.[8,19] $[\alpha]_D^{20} = +32.6$ (*c* 3.5, EtOH). Elem. Calcd: C, 71.40; H, 8.50; N, 9.20. Found: C, 70.97; H, 8.90; N, 9.15.

4.2.2. (1*R*,2*R*)-2-Amino-1-phenyl-1-propanol 1b. Granular white crystals (1.792 g) were produced from 3 g of (1*S*,2*R*)-norephedrine (60%). ^{1}H NMR ($CDCl_3$): δ 0.95 (d, 3H, $J = 6.64$ Hz), 3.02 (quintet, 1H, $J = 6.44$ Hz), 3.12 (s, 1H), 4.24 (d, 1H, $J = 7.03$ Hz), 7.23–7.33 (m, 5H). ^{13}C $\{^{1}H\}$ NMR ($CDCl_3$): δ 19.9, 52.9, 78.5, 126.6, 127.5, 128.3, 142.5. FT-IR (nujol): 1456, 1041, 749, 699. Mp = 71–73 °C. $[\alpha]_D^{28} = -31.4$ (*c* 3.49, EtOH), lit.[8,20] $[\alpha]_D^{20} = -32.6$ (*c* 3.5, EtOH). HRMS (M+1): calcd: 152.1078, found: 152.1075.

4.3. Preparation of (5*S*,4*S*)-4-methyl-5-phenyl-2-oxazolidinone 5a

Methylene chloride was added to (1*R*,2*S*)-norephedrine (2 g, 12.1 mmol) to afford approximately a 0.3 M solution. To this solution, was added triethylamine (1.85 mL, 13.31 mmol) and the reaction was cooled in an ice bath. Upon sufficient cooling, di-*tert*-butyl dicarbonate (2.68 g, 12.3 mmol) was added and the ice removed after the di-*tert*-butyl dicarbonate was dissolved (approximately 5 min). The reaction was allowed to proceed for 2 h at ambient temperature. The reaction was again cooled in an ice bath and an additional portion of triethylamine (1.85 mL, 13.3 mmol) was added followed by an addition of methanesulfonyl chloride (1.41 mL, 18.2 mmol) and the ice was removed after 5 min. The reaction was then

refluxed for 3 h at which time the reaction was allowed to cool to room temperature. Oxazolidinone **5a** was washed with bicarbonate and brine solutions and the solvents removed. The resulting orange crystals were triturated in diethyl ether to afford **5a** as granular white crystals in 82% yield. ^{1}H NMR ($CDCl_3$): δ 1.39 (d, 3H, $J = 6.25$ Hz), 3.84 (quintet, 1H, $J = 6.45$ Hz), 5.04 (d, 1H, $J = 7.42$), 7.35–7.42 (m, 5H). ^{13}C {^{1}H} NMR ($CDCl_3$): δ 19.8, 56.5, 85.3, 125.8, 128.7, 128.8, 137.6, 159.4. FT-IR (Nujol)—3275, 1704, 1456, 767, 700. Mp = 121–123 °C lit.[12] 117–119 °C. $[\alpha]_D^{29} = +21.6$ (c 2.3, $CHCl_3$) lit.[12] $[\alpha]_D^{21} = +29.5$ (c 2.3, $CHCl_3$). HRMS (M+1) calcd: 178.0858, found: 178.0868.

4.4. Formation of (5*S*,4*R*)- and (5*R*,4*S*)-oxazolidinones

Racemic norephedrine was reacted with diethyl carbonate and lithium hydride in hexanes to afford a white solid whose ^{1}H NMR matched the enantiomerically enriched oxazolidinones. This racemic oxazolidinone was used for HPLC studies on compounds **5a** and **5b**. Additionally, a sample of (1*R*,2*S*)-norephedrine was converted to the corresponding (5*R*,4*S*)-oxazolidinone **6a** in the same manner and used for HPLC analysis of **5a** only.

4.5. HPLC studies

Crude samples of the oxazolidinone were obtained either after the extraction of the oxazolidinone or from samples taken from the one-pot synthesis prior to the addition of the aqueous LiOH solution. These were not extracted prior to HPLC analysis, only the THF was removed under vacuum.

Crude HPLC (4*S*,5*S*)-oxazolidinone from **5a** CH_2Cl_2 synthesis (Dynamax-100 Å) in a 1:1 hexanes–ethyl acetate solvent system. $t_{R1} = 10.0$ min (**5a**), 95%; $t_{R2} = 12.8$ min, 5% (**6a**). Sample spiked with (5*R*,4*S*)-oxazolidinone (**6a**) (Dynamax-100): $t_{R1} = 9.83$ min, 32% (**5a**); $t_{R2} = 12.17$ min, 68% (**6a**).

Crude chiral HPLC (4*S*,5*S*)-oxazolidinone **5a** from one-pot synthesis (Chiracel-OD) in a 9:1 hexanes–isopropanol solvent system. $t_{R1} = 11.25$ min (**5a**), >99%; $t_{R2} = 13.33$ min, <1% (**5b**); racemic $t_{R1} = 11.17$ min (**5a**), 50%; $t_{R2} = 13.41$ min, 50% (**5b**).

Crude chiral HPLC (4*R*,5*R*)-oxazolidinone **5b** from one-pot synthesis (Chiracel-OD) in a 9:1 hexanes–isopropanol solvent system. $t_{R1} = 12.08$ min (**5a**), 1%; $t_{R2} = 13.83$ min, 99% (**5b**), mixture of **5a** and **5b** in a 92:8 hexanes–isopropanol solvent system: $t_{R1} = 13.83$ min, 51% (**5a**); $t_{R2} = 16.83$ min, 49% (**5b**).

4.6. X-ray crystal structure data for 1a

X-ray quality crystals were grown by vapor slow diffusion from ethyl acetate and hexanes. A colorless clear block thereby obtained of approximate dimensions $0.43 \times 0.40 \times 0.37$ mm^3 was mounted on a glass fiber with superglue and transferred a Bruker CAD4/Mach3 diffractometer equipped with a scintillation detector, and an Oxford Cryosystems Cobra Cryostream. Data were collected at 173 K using graphite-monochromated Mo Kα ($\lambda = 0.71073$ Å) radiation. A monoclinic unit cell with dimensions: $a =$ 5.4136(5) Å; $b = 7.5436(5)$ Å; 10.234(1) Å; $\beta = 91.525(9)$ was indexed from 25 reflections. Limiting indices for full data collection were as follows: $-7 \leqslant h \leqslant 7$, $-10 \leqslant k \leqslant 10$, $-13 \leqslant l \leqslant 13$. A total of 4424 reflections were collected, of which 1190 were unique, and 1144 were observed with $F_o^2 > 2\sigma(F_o^2)$. Systematic absences were consistent with either the $P2_1$ or $P2_1/m$ space groups. As the crystal contained an enantiomerically pure substance, the space group was conclusively determined to be $P2_1$. Data reduction, psi-scan absorption correction, solution, refinement, and data analysis were performed using the WinGX software package.[21] The structure was solved using the direct methods program SIR-2004.[22] The remaining atoms were located using difference Fourier synthesis, and full-matrix least-squares refinement on F^2 that led to a convergence was performed using SHELXL-97.[23] All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms attached to carbon atoms were assigned positions based on the geometries of their attached carbon atoms and were given isotropic thermal parameters 20% greater than their parent carbon atoms.

Full-matrix least-squares refinement on F^2 led to convergence with $R_1 = 0.029$ and $wR_2 = 0.083$ for 1144 data with $F_o^2 > 2\sigma(F_o^2)$. A final difference Fourier synthesis showed features in the range of +0.263 to −0.126 e$^-$/Å^3 and were deemed of no chemical significance. The use of Mo radiation precluded the collection of meaningful Friedel pairs, so absolute stereochemistry is known strictly from the synthetic method. The relative stereochemistry is conclusive as determined by crystallography. A RASTEP drawing[24] of the refined structure is shown in Figure 2. Complete X-ray structural data have been deposited at the Cambridge Crystallographic Data Center, CCDC No. 617758.[25] This X-ray structure for **1a** has previously been reported, although, only unit cell parameters, space group, and final R value were published.[26]

Acknowledgments

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