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Synthesis and determination of the absolute configuration of the enantiomers of modafinil

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Abstract—The asymmetric synthesis of both enantiomers of modafinil, a unique CNS stimulant with a reduced abuse liability, is described. This approach effectively prepares modafinil on a multigram scale in several steps from benzhydrol. The described synthetic route has also been used to produce the more water soluble analogue, adrafinil. X-ray crystallographic analysis on (−)-(diphenylmethanesulfinyl)acetic acid has determined the absolute configuration to be *R*.

1. Introduction

Narcolepsy is a sleep disorder that affects approximately 0.06% of the population in North America and Western Europe.[1] It is a disabling, neurological disorder that is characterized by chronic sleepiness and a marked disorganization of sleep/awake behavior.[2,3] Psychostimulants, such as amphetamine **1** and methylphenidate **2** (Fig. 1), are used clinically for treatment of narcolepsy,[1] as well as attention deficit/hyperactivity disorder (ADHD).[4] However, these agents are controlled substances with a potential risk of tolerance and dependence. Unfortunately, this often poses a substantial barrier to the use of these compounds for the drug treatment of these disorders.[5] As a result, there has been an effort to identify novel, nonstimulant treatments for narcolepsy and ADHD.

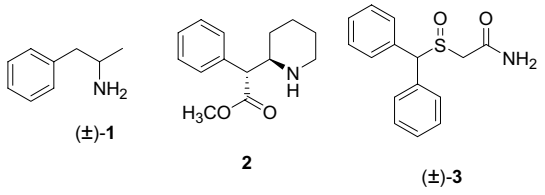

Figure 1. Structures of amphetamine (±)-**1**, methylphenidate **2**, and modafinil (±)-**3**.

Modafinil, [Provigil®, (2-(diphenylmethylsulfinyl)acetamide] (±)-**3** is a unique psychostimulant drug that has recently been approved by the Food and Drug Administration for the treatment of narcolepsy.[6] Recent work suggests that it might also be of utility as a treatment for ADHD,[4,5] and in treating opioid-induced sedation.[7]

Curiously, modafinil, unlike other CNS stimulants, has been reported to have little abuse liability.[8,9] However, it is not as potent as methamphetamine as a CNS stimulant.[8] Nevertheless, previous studies have shown that it promotes vigilance and wakefulness without the central and peripheral side effects associated with other psychostimulants, such as **1** and **2**.[10,11] Recent clinical work explores the possibility that due to its stimulant actions and low abuse potential, modafinil might represent a novel treatment for stimulant dependence.[12–14]

The mechanism through which (±)-**3** exerts its biological activity is only partially understood, however, its mechanism of action appears different than that of other CNS stimulants such as *d*-amphetamine.[10] For example, early reports indicated that (±)-**3** binds to the dopamine transporter (DAT),[15] while more recent work suggests that γ-aminobutyric acid (GABA) and/or serotonin (5-HT) receptors may also play a role in its mechanism of action.[16,17]

As part of our research to develop novel compounds to study the neurochemical mechanisms of drug abuse and drug dependence in the central nervous system, we decided to investigate further the structure–activity relationships of (±)-**3**.

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Modafinil contains an asymmetric sulfoxide functional group, but is prescribed clinically as a racemate. Both isomers are pharmacologically active and are presumed to contribute to the therapeutic effects of (±)-**3**.[18] However, the pharmacological properties of the two enantiomers are different.[19] It has been reported that *d*-modafinil is eliminated from the body three times faster than *l*-modafinil.[19] Interestingly, the absolute configuration of neither *l*-modafinil nor *d*-modafinil has been determined to date.

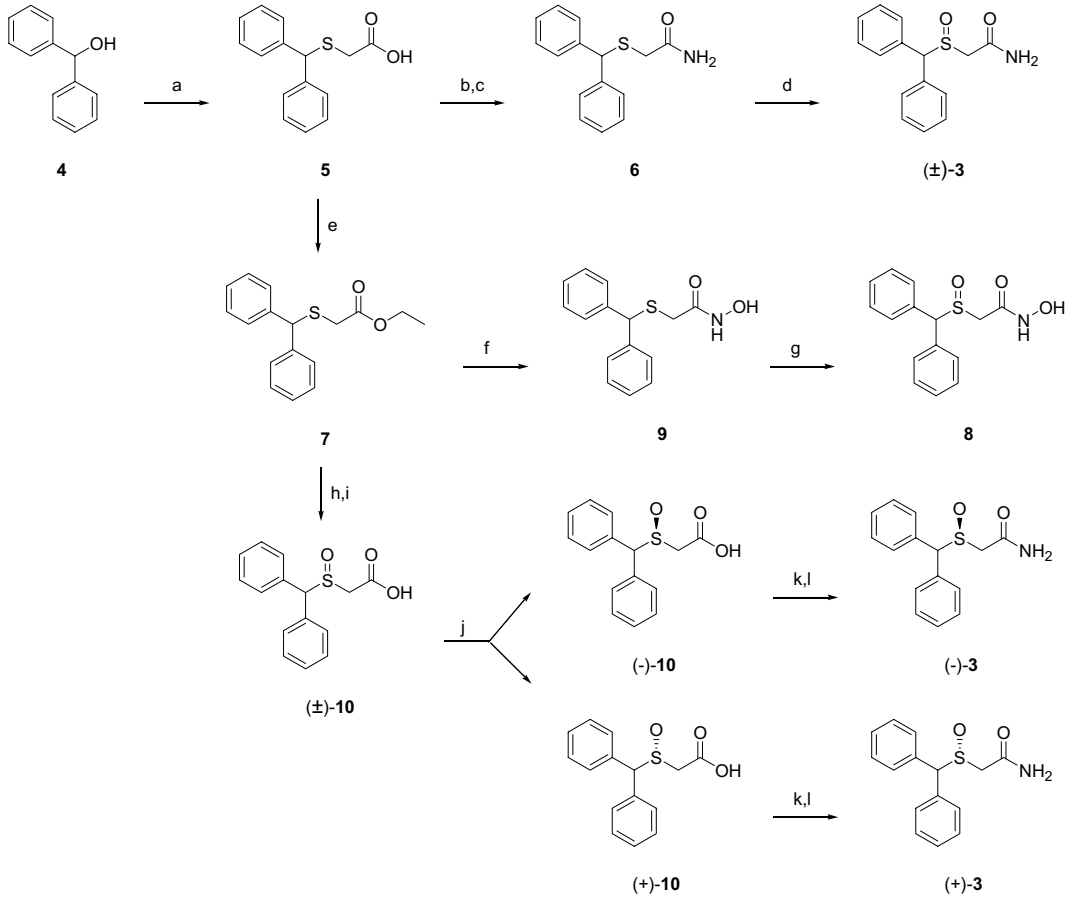
2. Results and discussion

As a first step into the investigation of the structure–activity relationships of modafinil, we aimed to develop a method for preparing multigram quantities of (±)-**3** by a route amendable to the production of various analogues. Moreover, we sought to determine the absolute configurations of the (−)-isomer and (+)-isomers of modafinil, (−)-**3** and (+)-**3**, respectively.

The synthesis of racemic modafinil, (±)-**3**, begins with the reaction of benzhydrol **4** and thioglycolic acid in trifluoroacetic acid to afford benzhydrylsulfanylacetic acid **5** in 99% yield (Scheme 1).[20,21] The reaction of acid **5** with thionyl chloride in benzene followed by treatment of the corresponding acid chloride[22] with concentrated ammonium hydroxide gave acetamide **6** in 87% yield.[22] Oxidation of the thioether moiety with 30% H_2O_2 in acetic acid produced (±)-**3** in 67% yield.[23]

After accomplishing our initial goal of finding an efficient synthesis of (±)-**3**, we focused on the preparation of (−)-**3** and (+)-**3**. Initially, we wished to synthesize these enantiomers using an enantioselective oxidation.[24–27] However, attempts to oxidize both **5** and **6** using (*S*,*S*)-(−)-diethyl tartrate, Ti(O-*i*-Pr)$_4$, and cumene hydroperoxide[28] proved unsuccessful. It was then decided that resolution via diastereomeric salt formation with α-methylbenzylamine and a carboxylic acid derived from (±)-**3** would be a more suitable route from which to prepare (−)-**3** and (+)-**3**.[29]

Unexpectedly, the hydrolysis of amide (±)-**3** to the corresponding acid, that is (±)-**10**, under both acidic and basic conditions resulted in mainly decomposition. Additionally, attempts at direct oxidation of **5** to (±)-**10**, as previously described,[20] were also unsuccessful. Furthermore, poor yields were seen if the oxidant changed from H_2O_2 to $NaIO_4$ or IBX.[30,31]



Scheme 1. Reagents and conditions. (a) Thioglycolic acid, TFA; (b) $SOCl_2$, Benzene; (c) NH_4OH, CH_2Cl_2; (d) H_2O_2, AcOH, 40 °C; (e) EtOH, concd H_2SO_4; (f) $NH_2OH{\cdot}HCl$, KOH, MeOH; (g) H_2O_2, AcOH, 60 °C; (h) H_2O_2, MeOH; (i) NaOH, H_2O, EtOH; (j) i. Fractional crystallization with α-methylbenzylamine; ii. concd HCl, H_2O; (k) Iodomethane, K_2CO_3, Acetone; (l) NH_4OH, NH_4Cl, MeOH.

In an attempt to evade this oxidation problem, the carboxyl group was protected as an ester, that is **7**. This allowed an opportunity to synthesize adrafinil **8**, an analogue of modafinil. Ethyl ester **7** was prepared smoothly from **5** under acidic conditions in 90% yield. The reaction of ester **7** with hydroxylamine under basic conditions afforded hydroxamic acid **9** in 92% yield. Oxidation of **9** using 30% H_2O_2 in acetic acid gave (±)-**8** in 72% yield. The oxidation of ester **7** to the corresponding sulfoxide using 30% H_2O_2[32] followed by ester hydrolysis gave (±)-**10** in 85% yield for the two steps. (±)-Modafinic acid **10** was separated into its isomers, (−)-**10** and (+)-**10**, using fractional crystallation with α-methylbenzylamine. The specific rotations in MeOH at 589 nM of (−)-**10** and (+)-**10** were found to be −39.1 and +40.2, respectively. Compounds (−)-**10** and (+)-**10** were then subjected to a sequence of ester formation[33] and ammonolysis to give (−)-**3** and (+)-**3** in 54% yield.[29]

To determine the absolute configuration of (−)-**10**, single crystal X-ray crystallographic analysis was performed (Fig. 2). The X-ray diffraction analysis indicated that (−)-**10** had an (*R*)-configuration. Therefore, (+)-**10** would have an (*S*)-configuration. Given that (−)-**3** and (+)-**3** were prepared from (*R*)-(−)-**10** and (*S*)-(+)-**10**, respectively, and since the stereogenic center was not modified in our synthesis, (−)-**3** and (+)-**3** must be (*R*)-(−)-**3** and (*S*)-(+)-**3**, respectively.

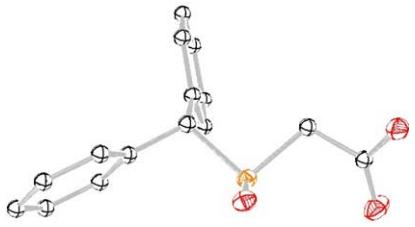


Figure 2. Displacement ellipsoid plot of (*R*)-(−)-**10** drawn at 35% probability levels.

3. Conclusions

Compounds (*R*)-(−)-**3** and (*S*)-(+)-**3** were prepared in an efficient method from benzhydrol by a process permitting a synthesis of multigram quantities. Research is currently underway to further examine the mechanism of action of (±)-**3**, (*R*)-(−)-**3**, (*S*)-(+)-**3**, and (±)-**10** in promoting wakefulness and their potential as stimulant abuse therapeutics.

4. Experimental section

4.1. Single-crystal X-ray diffraction analysis of (*R*)-(−)-10

A colorless prism was used for data collection with a Nonius KappaCCD detector on a kappa goniometer with sealed tube Mo source. The crystal was cooled with cold N_2 gas stream. Lattice parameters were determined using Scalepack[34,35] from 4556 reflections within $1.0 < \theta < 27.5°$. Data were collected to $2\theta = 55°$. A set of 30425 reflections was collected in the ϕ and ω scan mode. Empirical formula, $C_{15}H_{14}O_3S$. F_W (g/mmol), 274.32; temperature (K), 190; wavelength (λ, Å), 0.7107; trigonal space group P 3(2), unit cell dimensions: $a = b = 9.5840(10)$ Å, $c = 12.9863(13)$ Å; volume (Å^3), 1033.0(2); Z, 3; density (calculated) = 1.323 mg/mm^3, absorption coefficient (mm^{-1}), 0.235; $F(000) = 432$, crystal size (mm^3), $0.44 \times 0.37 \times 0.34$; Corrections were applied for Lorentz, polarization, and absorption effects. The structure was solved with XS and refined with XL of the SHELXTL v6.1[36] suite of programs. The full-matrix least-squares refinement on 3142 F^2 used 1 restraint and varied 178 parameters including atom coordinates and anisotropic thermal parameters. H atoms were included using a riding model [coordinate shifts of C applied to attached H atoms, C–H distances set to 0.98–0.93 Å, H angles idealized, U_{iso}(H) were set to 1.2–1.5U_{eq}(C). Final residuals were $R1 = 0.023$ for the 3005 observed data with $F_o > 4\sigma(F_o)$ and 0.059 for all data. Final difference Fourier excursions of 0.14 and −0.15 eÅ^{-3}. The assignment as (*R*)-(−)-**10** was confirmed by the Flack parameter[37] (0.01(4)). Coordinates of the compound has been deposited with the Cambridge Crystallographic Data Centre (Cambridge University Chemical Laboratory, Cambridge CB2 1EW, UK). CDCC number: 227059 and can be obtained free of charge.

4.2. General remarks

Optical rotations were determined on a Jasco P-1020 polarimeter at 589 nM and 22 °C. All melting points were determined on a Thomas–Hoover melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a Bruker Advance-300 instrument using $CDCl_3$ or DMSO-d_6 as solvent, δ values in ppm, and J (Hz) assignments of ^{1}H resonance coupling. Thin layer chromatography (TLC) was performed on 250 mm Analtech GHLF silica gel plates using either *n*-hexanes/ EtOAc, 4:1, *n*-hexanes/ EtOAc, 1:1 or CH_2Cl_2 / MeOH, 9:1 as elutent.

4.3. (Benzhydrylsulfanyl)acetic acid 5

A mixture of benzhydrol (50.0 g, 271.4 mmol) and thioglycolic acid (25.0 g, 271.4 mmol) in trifluoroacetic acid (300 mL) was stirred at room temperature for 3 h. The solvent was removed under reduced pressure to afford a crude solid. H_2O (300 mL) was added and the resulting precipitate collected by filtration. The solid was washed with hexanes (400 mL) and dried to afford 69.2 g (99 %) of **5** as a white solid, mp 126–129 °C (lit.[20,21] 123–124 °C): ^{1}H NMR (DMSO-d_6): δ 7.1–7.6 (m, 10H); 5.4 (s, 1H); 3.0 (s, 2H); ^{13}C NMR (DMSO-d_6): δ 171.5, 141.5, 129.3, 128.7, 128.0, 53.6, 34.4.

4.4. (2-Benzhydrylsulfanyl)acetamide 6

A solution of thionyl chloride (20 mL, 274.8 mmol) in benzene (20 mL) was added in a dropwise manner to a solution of **5** (19.5 g, 75.5 mmol) in benzene (114 mL) and the resulting mixture heated at reflux for 1.5 h. The solvent was removed under reduced pressure to afford a crude orange oil. A solution of the oil in CH_2Cl_2 (100 mL) was added cautiously to a vigorously stirred solution of concd NH_4OH (250 mL). The mixture was stirred vigorously for 2 h and the layers separated. The aqueous mixture was extracted with CH_2Cl_2 (2 × 50 mL). The combined CH_2Cl_2 portion was washed with 5% $NaHCO_3$ (3 × 75 mL) and saturated NaCl (100 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a crude solid that was recrystallized from isopropyl ether to give 17.0 g (87%) of **5** as a white solid, mp 109–110 °C (lit. 110 °C): ^{1}H NMR ($CDCl_3$): δ 7.3–7.4 (m, 10H); 6.5 (bs, 1H); 5.4 (bs, 1H); 5.2 (s, 1H); 3.0 (s, 2H); ^{13}C NMR ($CDCl_3$): 171.3, 140.2, 128.7, 128.2, 127.6, 54.7, 35.5.

4.5. [2-(Diphenyl)methanesulfinyl]acetamide (±)-3

A solution of **6** (14.4 g, 56.0 mmol) and 30% H_2O_2 (5.6 mL, 49.4 mmol) in acetic acid (60 mL) was stirred at 40 °C overnight. The mixture was poured into H_2O (200 mL) and a white precipitate formed. The solid was collected by filtration and recrystallized from MeOH to afford 10.2 g (67%) of (±)-**3** as a white solid, mp 162–163 °C (lit.[23] 164–166 °C): ^{1}H NMR (DMSO-d_6): δ 7.3–7.7 (m, 10H); 6.1 (s, 1H); 5.3 (s, 1H); 3.7 (s, 1H); 3.3 (d, J = 13.6 Hz, 1H); 3.2 (d, J = 13.6 Hz, 1H); ^{13}C NMR (DMSO-d_6): 166.3, 163.3, 137.2, 134.9, 133.2, 129.9, 129.7, 129.0, 128.8, 128.6, 128.5, 127.9, 127.9, 71.3, 68.7, 56.1, 55.8.

4.6. Ethyl (Benzhydrylsulfanyl)acetate 7

A mixture of **5** (70.0 g, 271.0 mmol), concd H_2SO_4 (10 mL), and absolute ethanol (600 mL) was heated at reflux overnight. The solvent was removed under reduced pressure and Et_2O (500 mL) added to the residue. The mixture was washed sequentially with H_2O (2 × 150 mL), 5% $NaHCO_3$ (1 × 150 mL), and saturated NaCl (200 mL), and then dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded 76.4 g (99%) of **7** as a clear oil: ^{1}H NMR ($CDCl_3$): δ 7.2–7.5 (m, 10H); 5.4 (s, 1H); 4.1 (q, J = 7.1 Hz, 2H); 3.1 (m, 2H); 1.2 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$): 170.1, 140.2, 128.4, 128.3, 127.3, 61.1, 53.9, 33.5, 14.0.

4.7. (±)-(Diphenylmethanesulfinyl)acetic acid (±)-10

A solution of 30% H_2O_2 (90.7 g, 801.0 mmol) was added in a dropwise manner to a solution of **7** (76.4 g, 267.0 mmol), absolute MeOH (600 mL), and acid catalyst (61.6 mL, prepared from 2-propanol (90 g), and concd H_2SO_4 (4 g)) at room temperature and the resulting solution stirred overnight. NaCl (200 g) was added and the mixture extracted with CH_2Cl_2 (3 × 200 mL). The combined CH_2Cl_2 portion was washed with saturated NaCl (100 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a crude solid that was used without further purification. A mixture of the crude solid NaOH (33.0 g, 825.0 mmol), absolute ethanol (800 mL), and H_2O (100 mL) was stirred at room temperature for 1 h. The solvent was removed under reduced pressure. H_2O (800 mL) was added to the residue and the aqueous mixture washed with Et_2O (2 × 200 mL). The mixture was made acidic (pH = 2) by the addition of concd HCl and the resulting precipitate collected by filtration and dried to afford 62.1 g (85%) of (±)-**10** as a white solid, mp 148–149 °C: ^{1}H NMR (DMSO-d_6): δ 13.2 (bs, 1H); 7.3–7.5 (m, 10H); 5.4 (s, 1H); 3.6 (d, J = 14.2 Hz, 1H); 3.3 (d, J = 14.2 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 168.0, 137.3, 135.5, 130.3, 129.8, 129.2, 129.1, 128.8, 128.7, 69.9, 56.1.

4.8. (*R*)-(−)-(Diphenylmethanesulfinyl)acetic acid (*R*)-(−)-10

A mixture of (*S*)-(−)-α-methylbenzylamine (29.4 g, 242.2 mmol) and (±)-**10** (62.1 g, 226.4 mmol) in H_2O (650 mL) was heated to reflux and then filtered. The filtrate was cooled slowly to room temperature. The resulting solid was collected by filtration and recrystallized two times from H_2O to afford 19.2 g (21%) of a white solid, mp 158–160 °C: $[\alpha]_D^{20}$ −67.2 (c = 1.05, MeOH). A suspension of the salt (19.2 g, 48.5 mmol) in H_2O (400 mL) was made acidic (pH = 2) by the addition of concd HCl. The resulting precipitate was collected by filtration and dried to afford 12.6 g (95%) of (*R*)-(−)-**10** as a white solid, mp 165–167 °C (lit.[29] 185–188 °C): $[\alpha]_D^{22}$ −39.1 (c = 1.06, MeOH); ^{1}H NMR (DMSO-d_6): δ 13.2 (bs, 1H); 7.3–7.5 (m, 10H); 5.4 (s, 1H); 3.5 (d, J = 14.3 Hz, 1H); 3.3 (d, J = 14.3 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 167.4, 136.6, 134.9, 130.3, 129.6, 129.1, 128.6, 128.5, 128.1, 128.0, 69.2, 55.4.

4.9. (*S*)-(+)-(Diphenylmethanesulfinyl)acetic acid (*S*)-(+)-10

A mixture of (*R*)-(+)-α-methylbenzylamine (23.2 g, 191.4 mmol) and (±)-**10** (50.0 g, 182.3 mmol) [prepared from the filtrate of (*R*)-(−)-**10**] in H_2O (650 mL) was heated to reflux and filtered. The filtrate was cooled slowly to room temperature. The resulting solid was collected by filtration and recrystallized three times from H_2O to afford 31.7 g (44%) of a white solid, mp 157–160 °C: $[\alpha]_D^{22}$ +64.0 (c = 1.02, MeOH). A suspension of the salt (25.2 g, 63.7 mmol) in H_2O (600 mL) was made acidic (pH = 2) by the addition of concd HCl. The resulting precipitate was collected by filtration and dried to afford 17.0 g (97%) of (*S*)-(+)-**10** as a white solid, mp 163–164 °C (lit.[29] 185–188 °C): $[\alpha]_D^{22}$ +40.2 (c = 1.11, MeOH). ^{1}H NMR (DMSO-d_6): δ 13.2 (bs, 1H); 7.3–7.5 (m, 10H); 5.4 (s, 1H); 3.5 (d, J = 14.1 Hz, 1H); 3.3 (d, J = 14.1 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 167.3, 136.6, 134.8, 129.6, 129.1, 128.5, 128.4, 128.1, 128.0, 69.2, 55.4.

4.10. (*R*)-(−)-[2-(Diphenyl)methanesulfinyl]acetamide (*R*)-(−)-3

A mixture of (*R*)-(−)-**10** (2.0 g, 7.3 mmol), iodomethane (1.1 g, 8.0 mmol), and K_2CO_3 (1.1 g, 8.0 mmol) in acetone (125 mL) was heated at reflux overnight. The solvent was removed under reduced pressure and H_2O added to the residue. The aqueous mixture was extracted with CH_2Cl_2 (350 mL). The combined CH_2Cl_2 portion was washed with saturated NaCl (100 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a crude solid that was recrystallized from isopropyl ether to afford 1.4 g (68%) of the corresponding methyl ester as a white solid, mp 106–108 °C (lit.[29] 109–110 °C). A mixture of the ester (2.0 g, 6.9 mmol), NH_4Cl (0.5 g, 8.5 mmol), concd NH_4OH (35 mL), and MeOH (10 mL) was stirred at room temperature overnight. The resulting precipitate was collected by filtration and recrystallized from diisopropyl ether to afford 1.1 g (55%) of (*R*)-(−)-**3** as a white solid, mp 156–157 °C (lit.[29] 153–154 °C): $[\alpha]_D^{22}$ −76.6 ($c = 1.0$, $CHCl_3$): ^{1}H NMR (DMSO-d_6): δ 7.3–7.6 (m, 10H); 7.1 (s, 1H); 5.6 (s, 1H); 5.2 (s, 1H); 3.5 (d, $J = 14.4$ Hz, 1H); 3.1 (d, $J = 14.4$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 166.4, 137.2, 134.9, 129.7, 129.0, 128.5, 128.0, 68.8, 56.2.

4.11. (*S*)-(+)-[2-(Diphenyl)methanesulfinyl]acetamide (*S*)-(+)-3

A mixture of (*S*)-(+)-**10** (1.0 g, 3.6 mmol), iodomethane (0.6 g, 4.0 mmol), and K_2CO_3 (0.7 g, 4.0 mmol) in acetone (80 mL) was heated at reflux overnight. The solvent was removed under reduced pressure and H_2O added to the residue. The aqueous mixture was extracted with CH_2Cl_2 (350 mL). The combined CH_2Cl_2 portion was washed with saturated NaCl (100 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a crude solid that was recrystallized from isopropyl ether to afford 0.7 g (65%) of the corresponding methyl ester as a white solid, mp 106–108 °C (lit.[29] 109–110 °C). A mixture of the ester (0.7 g, 2.3 mmol), NH_4Cl (0.2 g, 2.8 mmol), concd NH_4OH (15 mL), and MeOH (2 mL) was stirred at room temperature overnight. The resulting precipitate was collected by filtration and recrystallized from diisopropyl ether to afford 0.4 g (54%) of (*S*)-(+)-**3** as a white solid, mp 153–154 °C (lit.[29] 153–154 °C): $[\alpha]_D^{22}$ +76.7 ($c = 0.99$, $CHCl_3$): ^{1}H NMR (DMSO-d_6): δ 7.3–7.6 (m, 10H); 7.1 (s, 1H); 5.6 (s, 1H); 5.2 (s, 1H); 3.5 (d, $J = 14.4$ Hz, 1H); 3.1 (d, $J = 14.4$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 166.4, 137.2, 134.9, 129.7, 129.0, 128.5, 128.0, 68.8, 56.2.

4.12. 2-Benzhydrylsulfanyl-*N*-hydroxyacetamide 9

A solution of hydroxylamine hydrochloride (5.3 g, 75.6 mmol) in MeOH (40 mL) was added to a solution of potassium hydroxide (7.5 g, 133.7 mmol) in MeOH (40 mL). The resulting solution was then treated with a solution of **7** (10.8 g, 37.7 mmol) in MeOH (40 mL). The resulting mixture was stirred for 15 min and filtered to remove any solid material and then stirred at room temperature overnight. The solvent was removed under reduced pressure and H_2O added to the residue. The aqueous mixture was made acidic (pH = 2) by the addition of concd HCl. The resulting precipitate was collected by filtration and dried to afford 9.5 g (92%) of **9** as a white solid, mp 105 °C (lit.[23] 118–120 °C): ^{1}H NMR (DMSO-d_6): δ 10.6 (bs, 1H); 8.9 (bs, 1H); 7.1–7.5 (m, 10H); 5.4 (s, 1H); 3.4 (s, 2H); ^{13}C NMR (DMSO-d_6): δ 166.3, 141.8, 129.3, 128.7, 128.0, 127.9, 53.7, 32.7.

4.13. [2-(Diphenyl)methanesulfinyl]-*N*-hydroxy-acetamide (±)-8

A solution of **9** (5.0 g, 18.3 mmol) and 30% H_2O_2 (2.0 mL, 40 mmol) in acetic acid (50 mL) was stirred at 40 °C overnight. The mixture was poured into H_2O (mL) and a white precipitate formed. The solid was collected and recrystallized from a mixture of ethyl acetate/isopropyl alcohol, 3:2 to afford 3.8 g (72%) of (±)-**8** as a white solid, mp 156–157 °C (lit.[23] 159–160 °C): ^{1}H NMR (DMSO-d_6): δ 10.8 (bs, 1H); 9.1 (bs, 1H); 7.3–7.5 (m, 10H); 5.4 (s, 1H); 3.3 (d, $J = 13.2$ Hz, 1H); 3.0 (d, $J = 13.2$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 161.1, 137.0, 134.9, 129.7, 129.1, 128.5, 128.0, 69.0, 53.8.

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