5,5′-[(6-Methyl-3-pyridinyl)methylene]bis(2,4(1*H*,3*H*)-pyrimidinedione) (5a) was isolated by filtration from the reaction above: mp 300 °C; IR (KBr) 3450 (N–H), 1710 (C=O) cm^{-1}; ^1H NMR (80 MHZ, Me_2SO-d_6) δ 8.55 (d, $J_{6,4}$ = 2.5 Hz, 1 H), 8.3 (dd, $J_{4,3}$ = 8.0 Hz, $J_{4,6}$ = 2.5 Hz, 1 H) 7.75 (d, $J_{3,4}$ = 8.0 Hz, 1 H), 7.15 (d, $J_{6,NH}$ = 6 Hz, 2 H, pyrimidinyl, collapses to singlet on deuterium exchange), 5.15 (s, 1 H), 2.75 (s, 3 H); high-resolution mass spectrum, *m/e* calcd for $C_{15}H_{13}N_5O_4$ 327.097, found 327.097.

5,5′-(Phenylmethylene)bis(2,4(1*H*,3*H*)-pyrimidinedione) (10). Uracil (1.0 g, 8.9 mmol) and benzaldehyde (0.946 g, 8.6 mmol) were heated under refluxing concentrated hydrochloric acid (20 mL). After 2 h the solution was cooled to ambient temperature, and the white precipitate that formed was removed by filtration and dried under vacuum, 1.3 g (4.4 mmol, 93% based on uracil): mp >300 °C; IR (KBr) 3450 (N–H), 1750 and 1650 (C=O) cm^{-1}; ^1H NMR (80 MHz, Me_2SO-d_6) δ 7.25 (m, 5 H), 6.75(d, $J_{6,NH}$ = 6 Hz, 2 H), 5.05 (s, 1 H); high-resolution mass spectrum, *m/e* calcd for $C_{15}H_{12}N_4O_4$ 312.086, found 312.087.

Acknowledgment. We are indebted to the Analytical and Physical Chemistry Department for the analytical data: E. Reich for combustion analyses, David B. Staiger and Gary E. Zuber for NMR/IR spectra, and Walter P. Johnson and Gerald D. Roberts for mass spectra.

Registry No. **2**, 66-22-8; **3a**, 53014-84-9; **3b**, 13669-42-6; **3c**, 555-16-8; **3d**, 872-85-8; **3e**, 4363-93-3; **4a**, 83902-97-0; **4b**, 102396-61-2; **4c**, 102396-62-3; **4d**, 102396-63-4; **4e**, 102396-64-5; **5a**, 102396-65-6; **10**, 102396-66-7; benzaldehyde, 100-52-7.

Formation of the Neopinone/Codeinone Ring System via Intramolecular 1,6-Addition of an Amino Moiety to a Dienyl Ketone[1]

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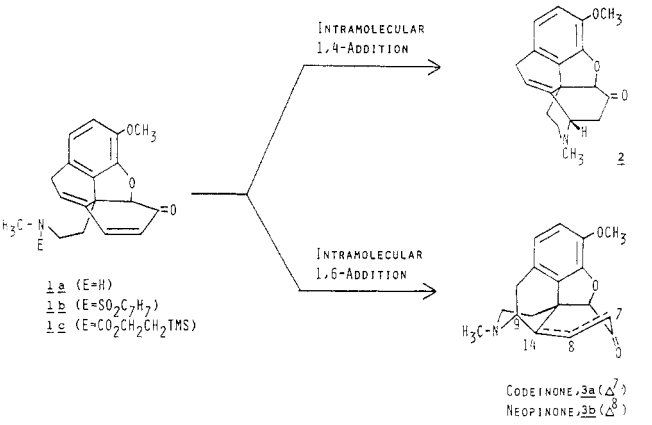
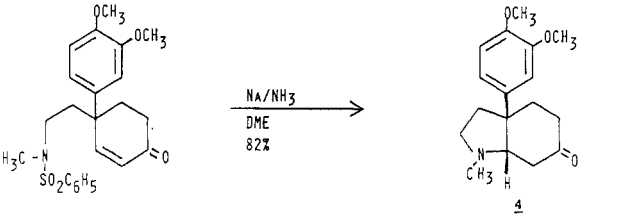
As part of a program directed toward the total synthesis of morphine and codeine[1] we wished to explore the possibility of effecting construction of the pentacyclic ring system via an intramolecular 1,6-addition of an amino residue to some suitably constituted dienyl ketone of the general type 1. Clearly the main issue is whether the desired addition mode (to afford **3a** or **3b**[2]) will be obtained in the presence of a potentially competitive 1,4-addition pathway (which would generate β-amino ketone **2**). Molecular models indicate that both pathways have excellent geometries and it seemed highly prudent to settle this question prior to the penultimate steps in a total synthesis (Scheme I).

For a number of reasons, we were initially attracted to examine a variant of the Sanchez reaction.[3] This reaction involves the direct reductive cyclization of sulfonamide enones under disolving metal conditions to afford β-amino ketones, as successfully demonstrated in the synthesis of (±)-mesembranone (**4**) (Scheme II). While the vinylogous reaction on a dienone like **1b** was unknown we felt it would be worth investigation. At the same time we also wished

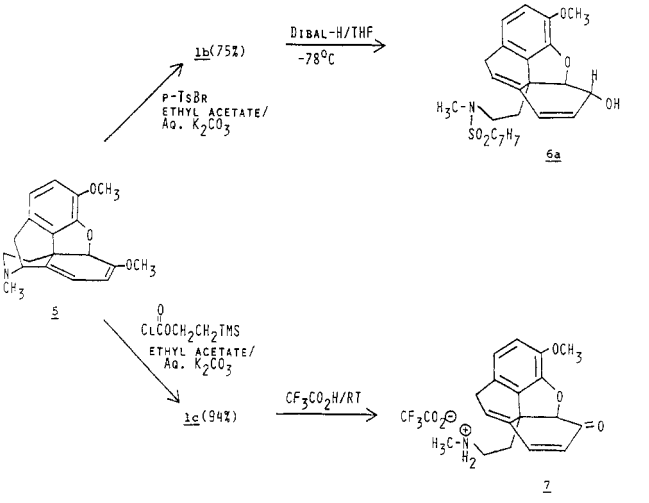
Scheme I



Scheme II



Scheme III



to prepare urethane **1c**, a progenitor of the parent amino dienone **1a**.

Treatment of thebaine (**5**)[4] with *p*-toluenesulfonyl bromide[5] (*p*-toluenesulfonyl chloride is ineffective in this reaction) under Schotten–Baumann acylation conditions, affords sulfonamide dienone **1b** in 75% yield. Unfortunately, reaction of **1b** under the dissolving metal conditions of Sanchez[3] yields an intractable mixture which did not exhibit a singlet methine resonance in the 4.3–5.3 ppm region of the 90-MHz NMR spectrum. In an effort to simplify the sulfonamide cleavage, dienone **1b** was reduced with DIBAL-H to generate dienyl alcohol **6a**[6] in 75% yield. Numerous attempts to desulfonylate this material under conditions previously shown to be effective at sulfonamide reduction[7] were either insufficient to effect cleavage or

(1) Morphine Support Studies. 2. For paper 1, see: Hamann, P. R.; Toth, J. E; Fuchs P. L. *J. Org. Chem.* **1984**, *49*, 3865.
(2) Barber, R. B.; Rapoport, H. *J. Med. Chem.* **1976**, *19*, 1175.
(3) (a) Sanchez, I. H.; Soria, J. J.; Larraza, M. I.; Flores, H. J. *Tetrahedron Lett.* **1983**, *24*, 551. (b) Sanchez, I. H.; Larraza, M. I.; Flores, H. J.; Diaz, E. *Heterocycles* **1985**, *23*, 593.
(4) Thebaine alkaloid powder, No. T-2019, Sigma Chemical Co., St. Louis, MO.
(5) Litvinenko, L. M.; Dadali, U. A.; Savelova, U. A.; Krichevtsova, T. I. *J. Gen. Chem. USSR (Engl. Transl.)* **1964**, *34*, 3780.
(6) Assignment of C-6 stereochemistry in **6a** is based on ^1H NMR coupling constants. See Experimental Section.

0022-3263/86/1951-2594$01.50/0

produced a myriad of products.

Faced with this problem we returned to thebaine (**5**) and effected nitrogen acylation with β-(trimethylsilyl)ethyl chloroformate[8] under the conditions employed by Bertgen, et al., with other chloroformates.[9,10] In contrast to their report,[9] the product **1c**, obtained in 94% yield, was assigned the $\Delta^{7,14}$-dienone structure on the basis of its NMR spectrum. Treatment of this urethane with neat trifluoroacetic acid at room temperature resulted in rapid evolution of carbon dioxide and afforded dienone **7** (Scheme III). Simple treatment of **7** with sodium bicarbonate produced a mixture of three compounds. Analysis by 470-MHz NMR demonstrated the kinetic control exerted by these cyclization conditions (1:6 **3a–3b**)[11] Purification of this mixture by silica gel chromatography produced a 1.5:1 ratio of **3a** to **3b** in 63% yield. Isolation of the third product [δ 4.60 (s), 5.43 (d, J = 6.0 Hz)] observed in the crude reaction mixture, which may be **2**, is currently being pursued.

Experimental Section

THF was distilled from benzophenone ketyl. Other reagents and solvents were used as purchased. Reactions were routinely monitored by TLC on precoated (0.25 mm) silica gel 60F-254 plates obtained from E. M. Reagents. Flash chromatography was performed on 230–400 mesh silica gel obtained from E. Merck. Melting points were obtained in open capillary tubes on a Thomas-Hoover apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer 1420 ratio recording infrared spectrophotometer using 10% solutions in $CHCl_3$. UV spectra were obtained on a Hewlett-Packard 8451A diode array spectrophotometer. Optical rotation was measured on an Autopol III instrument at ambient temperature. ^1H NMR spectra were obtained on a Nicolet 470-MHz instrument and a Perkin-Elmer R-32 90-MHz instrument using Me_4Si as an internal standard unless otherwise noted. ^{13}C NMR were obtained on a Varian XL-200 instrument (purchased with NSF Grant CHE-8004246) at 50 MHz using deuteriochloroform as the standard. Fully decoupled and APT spectra are reported. The latter are assigned an o (odd) for carbons with one or three attached hydrogens and e (even) for carbons with no or two attached hydrogens. Mass spectra were obtained by the Purdue University Mass Spectrometry Laboratory: low resolution on a Finnigan 4000 instrument with Nova 4 Data System (purchased with NSF Grant CHE-8010832) at 70 eV; high resolution on a Kratos MS 50 instrument.

3a(*R*),9b(*S*)-Dihydro-5-methoxy-9b-[2-[*N*-methyl-*N*-((4-methylphenyl)sulfonyl)amino]ethyl]phenanthro[4,4a,4b,5-*bcd*]furan-3(8*H*)-one (1b). A vigorously stirred biphasic mixture of thebaine (525 mg, 1.68 mmol) and potassium carbonate (700 mg, 5.06 mmol) in ethyl acetate (20 mL) and water (10 mL) was treated with *p*-toluenesulfonyl bromide[5] (395 mg, 1.68 mmol) in one portion. After 3.5 h, additional *p*-toluenesulfonyl bromide (200 mg, 0.85 mmol) was added. Three hours later, the organic layer was separated, washed with cold 3% hydrochloric acid solution (1×), water (3×), and saturated sodium chloride solution, and dried (sodium sulfate). Purification of the crude product by silica gel flash chromatography using a hexane–ethyl acetate gradient yielded 612 mg (80%) of **1b** as a thick oil: $[\alpha]^{25}_D$ −23.1° (c 1.21, $CHCl_3$); UV (EtOH) 284 nm (ε 8240); IR ($CHCl_3$) 5.95, 6.21, 6.69, 6.90, 7.46, 8.62, 9.09 μm; ^1H NMR (470 MHz, $CDCl_3$) δ 1.97–2.13 (m, 2 H), 2.41 (s, 3 H), 2.67 (s, 3 H), 2.85–2.95 (m, 1 H), 3.14–3.24 (m, 1 H), 3.38 (dd, 1 H, J = 6, 20 Hz), 3.55 (d, 1 H, J = 20 Hz), 3.86 (s, 3 H), 5.02 (s, 1 H), 5.94 (d, 1 H, J = 10.1 Hz), 6.36 (d, 1 H, J = 6 Hz), 6.67 (d, 1 H, J = 8 Hz), 6.72 (d, 1 H, J = 8 Hz), 7.24 (d, 1 H, J = 10.1 Hz), 7.29 (d, 2 H, J = 8 Hz), 7.57 (d, 2 H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 193.4 (e), 144.8 (e), 143.9 (o), 143.3 (e), 142.6 (e), 139.1 (e), 133.9 (e), 133.0 (o), 131.6 (e), 129.6 (o), 127.0 (o), 126.1 (e), 124.6 (o), 119.9 (o), 113.5 (o), 86.3 (o), 56.4 (o), 47.6 (e), 46.3 (e), 37.1 (e), 35.1 (o), 30.2 (e), 21.2 (o); mass spectrum, m/z (relative intensity) [CI] 452 (M^+ + 1, 100), 241 (33), 212 (45), 198 (33), [EI] 451 (M^+, 0.9), 239 (12), 212 (9), 155 (21), 139 (11), 91 (100); TLC (1:1 ethyl acetate–hexane) R_f 0.22; high-resolution mass spectroscopy (m/z) calcd for $C_{25}H_{25}NO_5S$ 451.1453, found 451.1445.

3a(*R*),9b(*S*)-Dihydro-5-methoxy-9b-[2-[*N*-methyl-*N*-(((2-(trimethylsilyl)ethyl)oxy)carbonyl)amino]ethyl]phenanthro[4,4a,4b,5-*bcd*]furan-3(8*H*)-one (1c). In the same manner as for **1b**, thebaine (2.0 g, 6.4 mmol), potassium carbonate (2.6 g, 19.3 mmol), and β-(trimethylsilyl)ethyl chloroformate[8] (1.25 mL, 6.8 mmol) yielded, after silica gel flash chromatography using a hexane–ethyl acetate gradient, 2.67 g (94%) of **1c** as a thick oil: $[\alpha]^{25}_D$ −59.4° (c 0.96, $CHCl_3$); UV (EtOH) 281 nm (ε 8750); IR ($CHCl_3$) 3.31, 3.38, 5.92, 6.67, 6.85, 6.94, 7.14, 7.81, 8.00, 8.59, 9.09, 11.63, 11.91 μm; ^1H NMR (470 MHz, $CDCl_3$, $CHCl_3$ reference δ 7.26) δ 0.00 (s, 9 H), 0.96 (t, 2 H, J = 9 Hz), 1.90–2.02 (br s, 1 H), 2.02–2.12 (m, 1 H), 2.79 (br s, 3 H), 3.10–3.46 (br m, 3 H), 3.55–3.65 (br d, 1 H), 3.84 (s, 3 H), 4.09 (t, 2 H, J = 9 Hz), 5.08 and 5.12 (both br s, 1 H, rotational isomerism of carbamate), 5.91 (d, 1 H, J = 10.0 Hz), 6.33 (d, 1 H, J = 6 Hz), 6.64 (d, 1 H, J = 8 Hz), 6.68 (d, 1 H, J = 8 Hz), 7.19 (d, 1 H, J = 10.0 Hz); ^{13}C NMR ($CDCl_3$) δ 193.6 (e), 156.1 (e), 144.9 (e), 143.7 (o), 142.7 (e), 139.4 (e), 132.7 (o), 131.9 (e), 126.0 (e), 124.7 (o), 119.8 (o), 113.5 (o), 86.6 (o), 63.3 (e), 56.5 (o), 47.7 (e), 45.0 (br, e), 36.7 (br, e), 34.1 (br, o), 30.3 (e), 17.6 (e), −1.7 (o); mass spectrum, m/z (relative intensity) [CI] 442 (M^+ + 1, 4), 414 (4), 370 (7), 313 (5), 174 (100), 158 (37) [EI] 441 (M^+, 5), 370 (7), 326 (14), 312 (31), 174 (100), 158 (37), 130 (12), 73 (55); TLC (1:4 ethyl acetate–chloroform) R_f 0.45; high-resolution mass spectroscopy (m/z) calcd for $C_{24}H_{31}NO_5Si$ 441.1971, found 441.1962.

3a(*R*),6(*R*),8,9b(*S*)-Tetrahydro-5-methoxy-6-hydroxy-9b-[2-[*N*-methyl-*N*-((4-methylphenyl)sulfonyl)amino]ethyl]phenanthro[4,4a,4b,5-*bcd*]furan (6a) and 3a(*R*),6(*S*),8,9b(*S*)-Tetrahydro-5-methoxy-6-hydroxy-9b-[2-[*N*-methyl-*N*-((4-methylphenyl)sulfonyl)amino]ethyl]phenanthro[4,4a,4b,5-*bcd*]furan. (6b). A solution of the dienone **1b** (630 mg, 1.40 mmol) in tetrahydrofuran (15 mL) under argon at −78 °C was treated dropwise with a DIBAL-H/hexane solution (1.6 mL, 1.6 mmol). When the addition was complete the reaction temperature was brought to −20 °C (methanol/ice bath). Fifteen minutes later, the mixture was poured into cold 5% hydrochloric acid solution and extracted with ethyl ether (2×) and dichloromethane (1×). The combined extract was washed with water (1×) and saturated sodium bicarbonate solution (1×) and dried (sodium sulfate). TLC analysis (1:1 ethyl acetate–hexane) indicated the production of a major (R_f 0.35) and minor (R_f 0.12) product. These were separated by silica gel flash chromatography using a hexane–ethyl acetate gradient.

Major product: **6a**, 494 mg (78%) as a colorless foam; $[\alpha]^{25}_D$ −41.6° (c 1.22, $CHCl_3$); IR ($CHCl_3$) 2.78, 3.31, 3.40, 5.95 (w), 6.25, 6.66, 6.90, 6.95, 7.46, 8.63, 9.16 μm; ^1H NMR (470 MHz, $CDCl_3$) δ 1.75–1.95 (m, 2 H), 2.42 (s, 3 H), 2.65 (s, 3 H), 2.83–2.93 (m, 1 H), 3.08–3.18 (m, 1 H), 3.25 (dd, 1 H, J = 6.5, 19.7 Hz), 3.41 (d, 1 H, J = 19.7 Hz), 3.87 (s, 3 H), 4.05 (d, 1 H, J = 7.5 Hz), 4.66 (d, 1 H, J = 7.5 Hz), 5.64 (d, 1 H, J = 9.9 Hz), 5.96 (d, 1 H, J = 6.5 Hz), 6.45 (dd, 1 H, J = 2.7, 9.9 Hz), 6.69 (d, 1 H, J = 8.0 Hz), 6.73 (d, 1 H, J = 8.0 Hz), 7.28 (d, 2 H, J = 8.1 Hz), 7.57 (d, 2 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 144.0 (e), 143.2 (e), 143.0 (e),

(7) (a) Buffered 6% sodium amalgam: Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477. (b) Lithium/ammonia: Donaldson, R. E.; Fuchs, P. L. *J. Org. Chem.* **1977**, *42*, 2032. (c) Sodium/ammonia: ref 3. (d) Sodium naphthalide: Closson, W. D.; Ji, S.; Schulenberg, S. *J. Am. Chem. Soc.* **1970**, *92*, 650. (e) Photolytic cleavage: Hamada, T.; Nishida, A.; Matsumoto, Y.; Yonemitsu, O. *J. Am. Chem. Soc.* **1980**, *102*, 3978.

(8) Carpino, L. A.; Tsao, J.-H.; Ringsdorf, H.; Fell, E.; Hettrich, G. *J. Chem. Soc., Chem. Commun.* **1978**, 358.

(9) (a) Bertgen, C.; Fleischhacker, W.; Vieböck, F. *Chem. Ber.* **1967**, *100*, 3002. While the authors report these products to be the $\Delta^{7,9}$-enones, we obtained the $\Delta^{7,14}$-dienones with benzoyl chloride, methyl chloroformate, benzyl chloroformate, trichloroethyl chloroformate, α-chloroethyl chloroformate, *p*-toluenesulfonyl bromide, and β-(trimethylsilyl)-ethyl chloroformate. (b) Allen, A. C.; Cooper, D. A.; Moore, J. M.; Teer, C. B. *J. Org. Chem.* **1984**, *49*, 3462.

(10) Attempted cleavage of the known[9] methylurethane dienone to **7** or **3** was unsuccessful.

(11) Authentic samples of codeinone,[12] neopinone,[2] and codeine[13] were prepared from thebaine for comparison purposes according to the literature procedures. Integration of the C-5 methine resonances, codeinone (δ 4.68), neopinone (δ 4.98), and unknown (δ 4.60), provided the relative ratios.

(12) Kotick, M. P.; Leland, D. L.; Polazzi, J. O.; Schut, R. N. *J. Med. Chem.* **1980**, *23*, 166.

139.0 (e), 134.5 (e), 132.2 (e), 129.6 (o), 129.1 (o), 127.8 (o), 127.5 (e), 127.2 (o), 124.2 (o), 119.9 (o), 112.6 (o), 94.7 (o), 70.3 (o), 56.4 (o), 46.7 (e), 46.4 (e), 36.7 (e), 35.0 (o), 29.5 (e), 21.4 (o); mass spectrum, m/z (relative intensity) [CI] 454 ($M^+ + 1$, 18), 436 (80), 298 (5), 251 (19), 212 (100), [EI] 298 (3), 241 (6), 155 (20), 91 (100); TLC (1:1 ethyl acetate–hexane) R_f 0.35; high-resolution mass spectroscopy (m/z) calcd for $C_{25}H_{27}NO_5S$ 453.1610, found 453.1590.

Minor product: **6b**, 32 mg (5%) as a colorless foam; $[\alpha]^{25}_D$ +13.2° (*c* 0.62, $CHCl_3$); IR ($CHCl_3$) 2.79, 3.31, 3.40, 5.95 (w), 6.02 (w), 6.25, 6.67, 6.85, 6.94, 7.46, 8.62, 9.09, 9.18 μm; ^1H NMR (470 MHz, $CDCl_3$) δ 1.78–1.96 (m, 2 H), 2.41 (s, 3 H) 2.64 (s, 3 H), 2.86–2.91 (m, 1 H), 3.08–3.13 (m, 1 H), 3.26 (dd, 1 H, J = 6.5, 19.6 Hz), 3.40 (d, 1 H, J = 19.6 Hz), 3.86 (s, 3 H), 4.51 (dd, 1 H, J = 4.6, 5.9 Hz), 4.80 (d, 1 H, J = 4.6 Hz), 5.95–5.99 (m, 2 H), 6.67 (s, 2 H), 6.70 (d, 1 H, J = 9.5 Hz), 7.28 (d, 1 H, J = 8.0 Hz), 7.57 (d, 1 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 145.6 (e), 143.2 (e), 142.0 (e), 138.8 (e), 134.5 (e), 133.4 (e?), 132.7 (o), 129.5 (o), 127.1 (o), 126.8 (e), 125.6 (o), 124.8 (o), 119.7 (o), 112.7 (o), 88.4 (o), 63.9 (o), 56.4 (o), 46.5 (e), 45.6 (e), 37.4 (e), 34.8 (o), 29.5 (e), 21.3 (o); mass spectrum, m/z (relative intensity) [CI] 454 ($M^+ + 1$, 19) 436 (40), 251 (24), 212 (100), 157 (28), 89 (16), [EI] 453 (M^+, 11), 298 (21), 268 (19), 241 (78), 198 (35), 181 (25), 155 (38), 91 (100), 58 (52); TLC (1:1 ethyl acetate–hexane) R_f 0.12; high-resolution mass spectroscopy (m/z) calcd for $C_{25}H_{27}NO_5S$ 453.1610, found 453.1609.

3a(*R*),9b(*S*)-Dihydro-5-methoxy-9b-[2-(*N*-methylammonio)ethyl]phenanthro[4,4a,4b,5-*bcd*]furan-3(8*H*)-one Trifluoroacetate (7). The dienone **1c** (90 mg, 0.20 mmol) was dissolved in trifluoroacetic acid (2 mL) at room temperature. Evaporation of the reaction solution, after 1 min, gave spectrally homogeneous amine salt **7**: ^1H NMR (470 MHz, $CDCl_3$/Me_2SO-d_6) δ 2.12–2.22 (m, 1 H), 2.22–2.32 (m, 1 H), 2.64 (br s, 3+ H), 2.90 (br s, 1 H), 3.06 (br s, 1 H), 3.38 (dd, 1 H, J = 6.1, 20.0 Hz), 3.59 (d, 1 H, J = 20.0 hz), 3.82 (s, 3 H), 5.15 (s, 1 H), 5.92 (d, 1 H, J = 10.1 Hz), 6.12 (br s, 4 H), 6.41 (d, 1 H, J = 6.1 Hz), 6.68 (d, 1 H, J = 8.1 Hz), 6.74 (d, 1 H, J = 8.1 Hz), 9.19 (br s, 1 H), 9.38 (br s, 1 H); ^{13}C NMR ($CDCl_3$/Me_2SO-d_6) δ 193.2 (e), 144.1 (e), 143.3 (o), 141.8 (e), 137.6 (e), 133.5 (o), 130.2 (e), 125.9 (e), 123.9 (o), 119.6 (o), 112.7 (o), 85.7 (o), 55.5 (o), 46.6 (e), 44.7 (e), 34.2 (e), 32.3 (o), 29.5 (e). In practice, **7** was used directly after preparation.

Biphasic Cyclization of 7. The salt **7** prepared from dienone **1c** (400 mg, 0.91 mmol) was taken up in chloroform and added to a vigorously stirred biphasic mixture of chloroform/saturated sodium bicarbonate solution (10 mL each). After 20 min, the organic layer was separated and the aqueous phase extracted with dichloromethane (4×). The combined extract was dried over sodium sulfate and yielded 260 mg of amber glass. ^1H NMR (470 MHz, $CDCl_3$) analysis of this material showed the presence of three major products, neopinone–codeinone–unknown (10.0:1.7:1.9);[11] This material was purified by flash chromatography on acetone-deactivated silica gel (5%) using a chloroform–methanol gradient to give 170 mg (63%) of an amber semicrystalline material, which analyzed as neopinone–codeinone (1:1.5) by 470-MHz ^1H NMR: TLC (85:15 chloroform–methanol) R_f 0.35.

Such mixtures could be isomerized to codeinone by the method of Rapoport.[2] For example, 220 mg of a neopinone–codeinone mixture in dichloromethane (4 mL) under argon was treated with a solution of hydrogen chloride in ether (5.5 M, 0.55 mL). After 30 min at room temperature the mixture was partitioned between dichloromethane and 0.2 N sodium hydroxide solution (40 mL). The aqueous phase was extracted with several portions of dichloromethane and the combined extract washed with water (1×) and dried over sodium sulfate. The amber glass obtained by evaporation was reduced with sodium borohydride (100 mg) according to Gates[13] to yield 200 mg of codeine as a tan glass, homogeneous by 90-MHz ^1H NMR. Recrystallization from ether/chloroform/cyclohexane gave a tan powder, mp 151.5–153 °C (lit.[13] mp 157–158.5 °C).

Acknowledgment. We thank the NIH (GM 3269302) for the funds to support this research program and the Purdue University Biological Magnetic Resonance Laboratory (NIH RR01077) for access to the 470-MHz ^1H NMR spectrometer. We also thank T. Braish and M. Anderson for 470-MHz ^1H NMR spectra.

(13) Gates, M. *J. Am. Chem. Soc.* **1953**, *75*, 4340.

Lanthanides in Organic Synthesis. 4. Reduction of α,β-Epoxy Ketones with Samarium Diiodide. A Route to Chiral, Nonracemic Aldols

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We recently described reduction of α-heterosubstituted ketones to the corresponding unsubstituted ketones utilizing samarium diiodide (SmI_2).[1] A variety of heterosubstituents can be reductively cleaved by this procedure under exceedingly mild conditions. Similar procedures applied to α,β-epoxy ketones result in formation of β-hydroxy ketones (aldols), of intense interest as key intermediates in construction of a variety of important natural products. Several methods have previously been developed for this particular process. Use of chromium(II) salts[2] and zinc/acetic acid,[3] as well as electrochemical methods,[4] often result in formation of enone or other byproducts, with corresponding decreases in yields of desired β-hydroxy ketones. Direct hydrogenation[5] has also been utilized, but the scope of this particular procedure has not been adequately delineated. At present, Al/Hg,[2h-j,6] NaTeH,[7] or NaI/NaOAc[8] appear to be reagents of choice for this particular transformation.

General interest in use of epoxides as intermediates in organic synthesis has intensified as a direct result of the development of the Sharpless asymmetric epoxidation reaction.[9] This procedure allows generation of chiral, nonracemic α,β-epoxy alcohols possessing several different

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