81522-68-1; **12**, 95716-68-0; **14**, 39903-97-4; **15** (isomer 1), 81570-18-5; **15** (isomer 2), 81570-19-6; **16**, 81506-17-4; **17**, 81506-18-5; **18**, 81506-19-6; **19**, 81506-20-9; **21**, 81506-21-0; **22**, 81506-22-1; **23**, 81506-23-2; **24**, 81570-20-9; **25**, 81506-24-3; **26**, 81506-25-4; **28**, 100928-03-8; **29**, 100928-04-9; **30**, 27943-46-0; **31**, 103095-15-4; **32**, 103095-16-5; **33**, 66774-84-3; **34**, 81506-41-4; **35**, 103189-00-0; **35i**, 83872-38-2; **36**, 924-50-5; **37**, 103189-01-1; **37i**, 103189-73-7; **38**, 95716-62-4; **38i**, 103095-18-7; **39**, 95716-63-5; **40**, 95716-64-6; **41**, 95716-65-7; **42**, 95716-66-8; **43**, 95716-67-9; **44**, 95716-69-1; **45**, 103095-17-6; $(EtO)_2POCH_2CO_2Et$, 867-13-0; Ph_2PLi, 4541-02-0; *tert*-butyldimethylsilyl chloride, 18162-48-6; *N*-(trimethylsilyl)-imidazole, 18156-74-6.

An Asymmetric Synthesis and Absolute Configuration of (*S*)-(−)-Deplancheine

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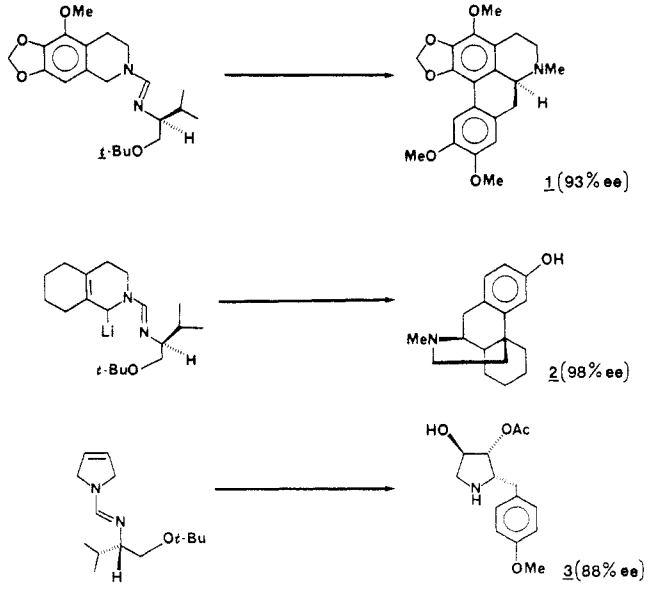
An asymmetric synthesis of (*S*)-(−)-deplancheine has been achieved in 96.5% ee via the chiral valine-based formamidine **8** of β-carboline. Alkylation of the latter, via its lithio salt, with the appropriate alkyl bromide **19c** gave the highly enantioenriched intermediate **20**, which was carried forward to the title product. On the basis of the stereochemical properties of deplancheine, the original assignment of absolute configuration (*S*) has now been reassigned as *R*-(+).

In our continuing study to evaluate the synthetic utility of α-amino carbanions derived from achiral and chiral formamidines,[1] we have been fortunate to reach a number of naturally occurring compounds in high enantiomeric purity. Additional achievements, since the review report, focused on the asymmetric total synthesis of the aporphine alkaloid (+)-ocoteine (**1**),[2] the morphinan dextrorphan (**2**),[3] and the antibiotic anisomycin **3**, as its unnatural antipode.[4] These processes occur with high asymmetric induction and involve relatively few synthetic steps, making this route to alkaloids one of considerable efficiency.



We now report that indole alkaloids are also accessible via the chiral formamidines, and to demonstrate this we have prepared the alkaloid (−)-deplancheine in greater than 95% ee and established the correct absolute configuration as *R*-(+).

(+)-Deplancheine (**4**) was recently isolated[5] from the New Caledonian plant *Alstonia deplanchei* van Heurck et Mueller Arg. (Apocyanaceae) and assigned the *S* configuration on the basis of an analogy with the majority of indole alkaloids. After its structure elucidation, a number

(S)-4 (R)-4

of total syntheses were reported,[6] while one synthesis was described before it was known as a natural product.[7] However, all of the synthetic approaches led to racemic material, thus no question regarding its absolute configuration became an issue. During the course of the asymmetric synthesis of **4**, we were forced to the conclusion that the original assignment was incorrectly made and that natural deplancheine possesses the *R* configuration. The synthesis of (*S*)-(−)-deplancheine has been performed by using two slightly different routes which differ markedly in their overall yield and these will be described herein.

In our anticipated scheme to reach deplancheine, we felt that β-carboline (**5**) would serve as an appropriate starting point.[8] Thermal exchange with the *N*,*N*-dimethylformamidine of (*S*)-*tert*-butylvalinol[3b] afforded the chiral carboline derivative **7** in 80% yield. The indole nitrogen was protected as its methoxymethyl ether by using potassium

(1) For a review of earlier work, see: Meyers, A. I. *Aldrichimica Acta* **1985**, *18*, 59.
(2) Dickman, D. A.; Meyers, A. I. *Tetrahedron Lett.* **1986**, *27*, 1465.
(3) (a) Meyers, A. I.; Bailey, T. R. *J. Org. Chem. 1986*, *51*, 872. (b) Meyers, A. I.; Dickman, D. A.; Bailey, T. R. *J. Am. Chem. Soc.* **1985**, *107*, 7974.
(4) Meyers, A. I.; Dupre, B. *Heterocycles*, in press.
(5) Besselievre, R.; Cosson, J. P.; Das, B. P.; Husson, H. P. *Tetrahedron Lett.* **1980**, *21*, 63.
(6) (a) Ashcroft, W. R.; Joule, J. A. *Tetrahedron Lett.* **1980**, *21*, 2341. (b) Hamelia, M.; Lounasmaa, M. *Acta. Chem. Scand., Ser. B* **1981**, *35*, 217. (c) Overman, L. E.; Malone, T. C. *J. Org. Chem.* **1982**, *47*, 5297. (d) Calabi, L.; Daniel, B.; Lesma, G.; Palmisano, G. *Tetrahedron Lett.* **1982**, *23*, 2139. (e) Rosenmund, R.; Casutt, M. *Tetrahedron Lett.* **1983**, *24*, 1771.
(7) Thielke, D.; Wegner, J.; Winterfeldt, E. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 602.
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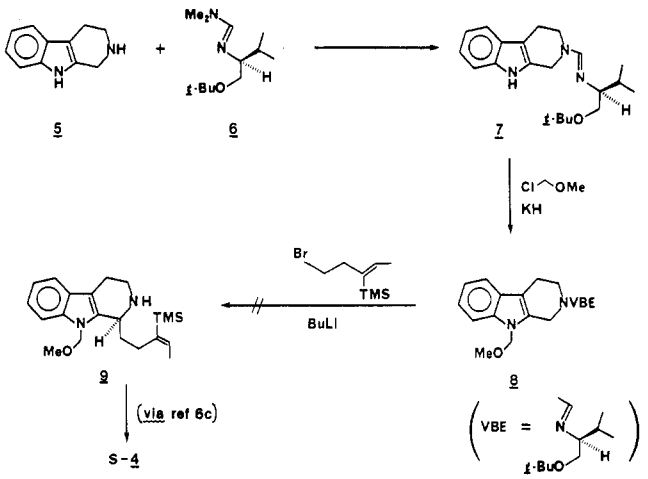
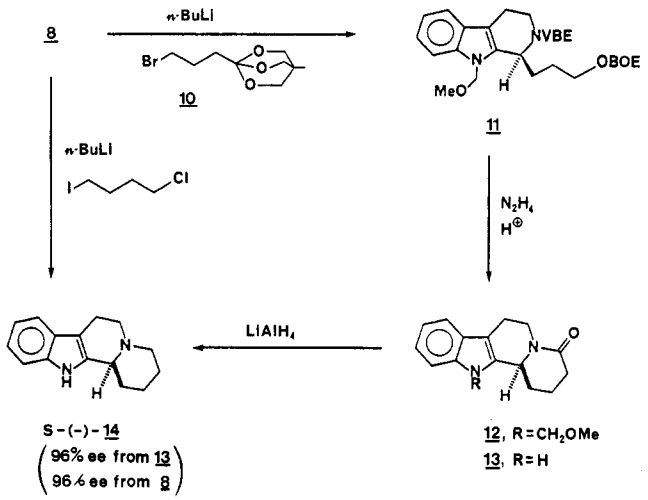
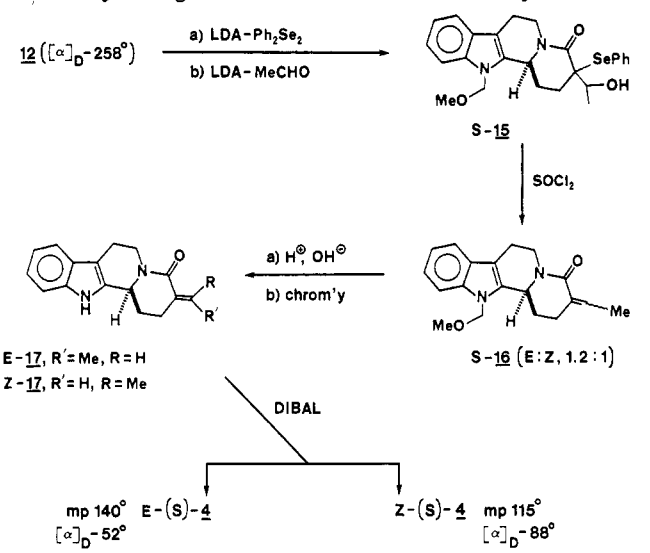


hydride–TMEDA and furnished the key precursor 8 to the indole alkaloids. Our initial effort required that the lithiated carboline react with the (*Z*)-bromovinylsilane to produce **9** and then proceed to induce an iminium ion–vinylsilane cyclization so elegantly demonstrated by Overman.[6c] However, no meaningful alkylation to **9** occurred, and this route was abandoned. The sequence to deplancheine was altered by alkylation of lithiated **8** with 1-(3-bromopropyl)-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (OBOE ester) (**10**),[9] affording the alkylated carboline **11**, which after hydrazine–acetic acid treatment gave the lactam **12** in 85% yield. Hydrolysis of the MOM group led to **13** in 94% yield. In order to assess the enantiomeric



purity of **13**, it was reduced ($LiAlH_4$) to the indoloquinolizidine **14**, a known indole alkaloid.[10] The product was identical in all respects with the natural *S*-(−) enantiomer and, on the basis of optical rotation, was 96% ee. The same quinolizidine **14** was prepared, as previously described,[11] by alkylation of **8** with 4-iodo-1-chlorobutane, also providing the product as the *S*-(−) enantiomer in 96% ee. With the absolute configuration of **13** firmly established as *S*, the sequence to deplancheine was continued. Introduction of the ethylidene group was performed[12] via the α-selenide and the α-lithioselenide by reaction with acetaldehyde to give **15**. Elimination with thionyl chloride



gave approximately a 1:1 mixture of the ethylidene lactams (*E*)- and (*Z*)-**16**, which was treated with acid and base to remove the MOM group, furnishing the mixture of (*E*)- and (*Z*)-**17**. Column chromatography gave pure (*E*)-**17** and (*Z*)-**17**, each of which were reduced separately with diisobutylaluminum hydride in toluene to give (*E*)-(*S*)-(−)-deplancheine [(*E*)-**4**], mp 139–140 °C, $(\alpha)_D$ −52.0°, and (*Z*)-(*S*)-(−)-deplancheine [(*Z*)-**4**], mp 115 °C, $[\alpha]_D$ −88°, respectively. This study, which led to the (*E*)-(−) enantiomer of **4** is confirmed as the *S* configuration on the basis of the *S* configuration of **13** and **14**. Thus, the *E*-(+) enantiomer, reported for natural deplancheine must have the *R* configuration. With regard to the discrepancy in the melting point of (*Z*)-**4** (mp 115 °C, $[\alpha]_D$ −88°) we found that (*Z*)-**4** melts initially at 115 °C, resolidifies at 123 °C, and remelts at 165 °C thus exhibiting polymorphic properties. It should be noted that no chemical change occurred during melting as evidenced by the fact that both (*E*)- and (*Z*)-**4** were purified by sublimation at 140 °C prior to taking their melting points and $[\alpha]_D$ values. This precludes the racemization of (*Z*)-**4**, which coincidentally has a mp of 165 °C for the reported racemate (mp 163 °C).[6c]

Although not common among indole alkaloids that are derived from amino acids, the *R* configuration at C-3 has been attributed to the enzyme biogenesis of these alkaloids.[5,13] In addition, the NMR spectrum of the (*E*)- and (*Z*)-deplancheine was of no assistance in assignment since they are very close and only a sample of (*R*)-(+)-deplancheine would clarify the problem of melting points.[13]

In summary of this discrepancy, it is felt that the *S*-(−) enantiomer of deplancheine has been assigned on a firm basis and the melting point of 139–140 °C is in fact that of the *S*-(−) enantiomer. It follows that the melting point of the *R*-(+) enantiomer must also be 140 °C while the racemate also melts at 140–143 °C.[6c]

Although we had demonstrated that the chiral formamidines are useful tools for the construction of indole alkaloids in high enantiomeric purity, we were not satisfied with the stage in the synthesis leading to a mixture of (*E*)- and (*Z*)-deplancheine (**4**). In this regard, we undertook an alternative approach which proved to be much more efficient and stereospecific providing (*S*)-(−)-deplancheine

(9) (a) Atkins, M. P.; Golding, B. T.; Howes, D. A.; Sellars, P. J. *J. Chem. Soc., Chem. Commun.* **1980**, 207. (b) Corey, E. J.; Natarajan, R. *Tetrahedron Lett.* **1983**, *24*, 5571.

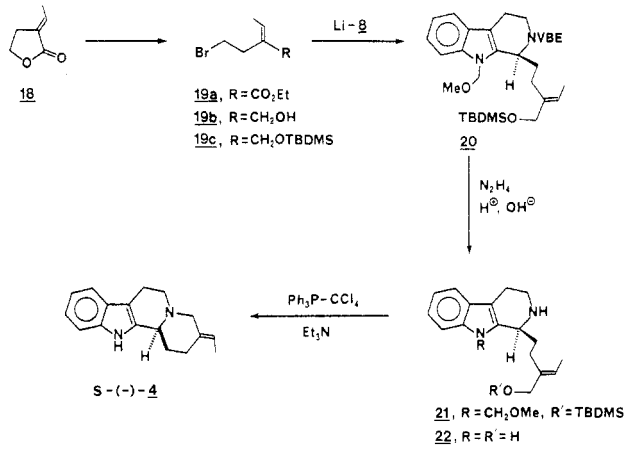
(10) Akimoto, H.; Okamura, K; Yui, M.; Shiori, T.; Kuramota, M.; Kikugawa, Y.; Yamada, S. *Bull. Soc. Chem. Jpn.* **1974**, *22*, 2614.

(11) Loewe, M. F.; Meyers, A. I. *Tetrahedron Lett.* **1985**, *28*, 3291.

(12) Reich, H. J.; Chow, F.; Shah, S. K. *J. Am. Chem. Soc.* **1979**, *101*, 6638. Remion, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1976**, 1385. Remion, J.; Krief, A. *Tetrahedron Lett.* **1976**, 3743.

(13) Fan, C.; Husson, H. P. *Tetrahedron Lett.* **1980**, *21*, 4265. In a private communication, Professor Husson has concurred with our assignment of natural deplancheine as *R*. With regard to the melting point discrepancy, Professor Husson has informed us that their supply of natural deplancheine has been exhausted.

without the contamination of the (*Z*)-ethylidene isomer. The most efficient route was considered to be that which incorporates the *E* double bond into the electrophile such that alkylation of the β-carboline formamidine would contain all the requisite carbon atoms. Starting with the 2-ethylidenebutyrolactone (**18**), prepared by the method of McMurray,[14] and treatment with ethanolic HBr gave the unsaturated *E* bromo ester **19a** in 61% yield. Reduction to the allylic alcohol **19b** was accomplished by using diisobutylaluminum hydride (94%) and masking the hydroxyl group as its *tert*-butyldimethylsilyl ether (66%) presented us with the appropriate alkyl halide **19c** necessary for asymmetric elaboration of the chiral β-carboline **8**. When the latter was metalated with *n*-butyllithium (−78 °C, THF) and treated with **19c**, the alkylated carboline **20** was isolated pure in 91% yield. The formamidine moiety was smoothly removed by using hydrazine–acetic acid ethanol after 1 h at room temperature, affording **21** in 92% yield after chromatography. The two protecting groups were simultaneously removed by successive treatment with THF–Et_2O (1:1) containing 3 N HCl and neutralization with aqueous KOH. This produced **22** in 64% yield as a crystalline material. The final transformation to (*S*)-(−)-deplancheine (**4**) was carried out with Ph_3P–CCl_4–Et_3N,[15] affording the product in 80% yield. Once again, the alkaloid exhibited $[\alpha]_D$ −52° and mp 140–142 °C, identical with those found in the synthesis of **4** from the lactam **12**. The synthesis of (*S*)-deplancheine was therefore accomplished in seven steps from the ethylidene lactone **18** and the β-carboline **8** in an overall yield of 16–17% and 96.5% ee.



In summary, this asymmetric synthesis has been shown to not only be a valuable endeavor in the acquisition of complex molecules of high enantiomeric purity but it is also quite important in establishing absolute configuration when a predictable stereochemical route is available. Additional indole alkaloid syntheses are in progress and will be reported in due course.

Experimental Section

The NMR spectra were determined on a Bruker-IBM 270-MHz instrument. Optical rotations were taken on a Rudolph Auto Pol polarimeter.

(*S*)-β-Carboline-*O*-*tert*-Butylvalinol Formamidine 7. To a 100-mL flask, equipped with a stir bar, condenser, and drying tube ($CaSO_4$) was added 50 mL of toluene. To this were added 3.0 g (18 mmol) of 1,2,3,4-tetrahydro-β-carboline (**5**), 3.17 g (18.4 mmol) of *N*-[(*N*,*N*-dimethylamino)methylene]-*O*-*tert*-butylvalinol[3b] (**6**), and 200 mg of camphorsulfonic acid. The solution was heated to reflux for 24–30 h and the solvent removed in vacuo. The residue, was taken up in 50 mL of ether, washed twice with 10% bicarbonate, dried (Na_2SO_4), and concentrated. The residue was chromatographed on aluminum oxide (1:1 hexane–ethyl acetate) to afford **7** as a white solid: 5.01 g (80%) mp 140–141 °C (ether); IR (KBr) 2955, 2850, 1636, 1420, 1185, 1065, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98 (s, 1 H), 7.45 (m, 2 H), 7.29 (m, 1 H), 7.11 (m, 2 H), 4.52 (s, 2 H), 3.53 (m, 3 H), 3.23 (m, 1 H), 2.77 (m, 3 H), 1.82 (m, 1 H), 1.13 (s, 9 H), 0.87 (d, *J* = 6.8 Hz, 6 H); ^{13}C ($CDCl_3$, ppm) 153.9, 136.0, 130.6, 127.0, 121.4, 119.3, 117.7, 110.7, 108.5, 72.6, 71.3, 64.9, 45.8, 42.2, 30.4, 27.7, 21.8, 20.8, 18.3; $[\alpha]_D^{20}$ −26.44° (*c* 1.18, $CHCl_3$).

(*S*)-9-(Methoxymethyl)-β-carboline-*O*-*tert*-Butylvalinol Formamidine 8. To excess KH (pentane washed) suspended in THF (40 mL), stirring in an ice bath, was added solid **7** (2.0 g, 5.8 mmol). The solution was stirred (30 min), TMEDA (0.75 g, 6.45 mmol) was added, and stirring was continued for an additional 30 min. Chloromethyl methyl ether (0.5 g, 6.45 mmol) was added, and the mixture was stirred (1 h), quenched with water, and warmed to room temperature. Extraction with ether, drying (K_2CO_3), and concentration gave a residue, which was chromatographed on silica gel (100:10 pentane–triethylamine) to yield **8** as a colorless oil (1.85 g, 82%): IR (neat) 2970, 1645, 1460, 1380, 1190, 1100, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47–7.39 (m, 3 H), 7.23–7.09 (m, 2 H), 5.36 (s, 2 H), 4.60 (m, 2 H), 3.68–3.48 (m, 3 H), 3.22–3.16 (m, 4 H), 2.80 (m, 3 H), 1.83 (m, 1 H), 1.12 (s, 9 H), 0.87 (m, 6 H); ^{13}C ($CDCl_3$, ppm) 153.7, 137.0, 132.1, 127.2, 121.6, 119.7, 117.8, 109.3, 109.2, 73.9, 72.4, 71.2, 64.8, 55.6, 45.3, 41.4, 30.2, 27.7, 21.7, 20.3, 18.2; $[\alpha]^{20}_D$ −24.07° (*c* 1.0, $CHCl_3$).

Anal. Calcd for $C_{23}H_{35}N_3O_2$: C, 71.68; H, 9.09; N, 10.90. Found: C, 71.39; H, 9.27; N, 10.75.

9-(Methoxymethyl)-β-carboline Lactam 12. To a stirring solution of **8** (527 mg, 1.37 mmol) in 14 mL of THF, cooled to −78 °C in dry ice–acetone, was added dropwise 0.8 mL of *n*-butyllithium (0.58 mL, 2.6 M hexane). The pale red solution was stirred for 1 h, and a solution of the bromo orthoester **10**[9] (375 mg, 1.5 mmol) in 10 mL of THF was added dropwise. After being stirred for 1 h, the solution was treated sequentially with 8 mL of 95% ethanol, 1 mL of H_2O, 1 mL of acetic acid, and 2 mL of hydrazine hydrate and allowed to stir for 4–5 h. Alternatively this hydrazine solution was stored in a freezer (0–3 °C) overnight. The reaction progress can be monitored by TLC (SiO_2, ethyl acetate–hexane). The solution was concentrated in vacuo and the residue taken up in ether, washed with water (3×), dried (K_2CO_3), and concentrated. Column chromatography (Al_2O_3) and elution with ethyl acetate–hexane (10:1) yielded 294 mg (84%) of **12**. Recrystallization from ethyl acetate afforded plate crystals (77%): mp 123–124 °C; IR (film) 2910, 2830, 1650, 1447, 1055, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (m, 1 H), 7.42 (m, 1 H), 7.22 (m, 2 H), 5.23 (s, 2 H), 5.18 (m, 1 H), 4.88 (m, 1 H), 3.29 (s, 3 H), 2.55–2.90 (m, 5 H), 2.48 (m, 1 H), 1.81–2.02 (m, 2 H), 1.70 (m, 1 H); $[\alpha]^{20}_D$ −258.0° ($CHCl_3$).

Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.8; H, 7.08; N, 9.85. Found: C, 71.64; H, 7.13; N, 9.53.

β-Carboline Lactam 13. The 9-(methoxymethyl)-β-carboline lactam **12** (275 mg) was dissolved in THF (4 mL) and treated with 20 mL of 3 N HCl. The mixture was stirred vigorously for 5 h and then rendered alkaline with 6 N KOH. Extraction with dichloromethane, drying (Na_2SO_4), and concentration gave a residue, which was chromatographed on silica gel (100:10:5 ethyl acetate–methanol–Et_3N), affording 260 mg (94%) of colorless crystals of **13**: mp 245–247 °C (lit.[16] mp 250 °C); IR ($CHCl_3$) 3460, 3260, 2990, 2910, 1615, 1455, 1190 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.29 (s, 1 H), 7.50 (d, *J* = 7.3 Hz, 1 H), 7.33 (d, *J* = 7.5 Hz, 1 H), 7.14 (m, 2 H), 5.15 (m, 1 H), 4.78 (m, 1 H), 2.77 (m, 3 H), 2.4–2.62 (m,, 3 H), 1.74–1.96 (m, 4 H); ^{13}C NMR ($CDCl_3$, ppm) 169.1, 136.1, 133.2, 126.7, 121.9, 119.6, 118.2, 110.8, 109.3, 54.4, 40.2, 32.5, 29.1, 21.0, 19.4; $[\alpha]^{20}_D$ −232.0° (*c* 1.02, $CHCl_3$).

(*S*)-(−)-1,2,3,4,6,7,12,12b-Octahydroindolo[2,3-*a*]quinolizine (14). To a stirring solution of **13** (106 mg, 0.44 mmol) in THF

(14) Ksander, G. M.; McMurray, J. E.; Johnson, M. *J. Org. Chem.* **1977**, *42*, 1180.

(15) Appel, R. *Angew, Chem., Int. Ed. Engl.* **1975**, *14*, 801. Stoilova, V.; Trifonov, L. S.; Orahovats, A. S. *Synthesis* **1979**, *105*. Okada, T.; Schimura, K.; Sudo, R. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1185. Meyers, A. I.; Hoyer, D. *Tetrahedron Lett.* **1985**, *39*, 4687.

(16) Massiot, G.; Malumba, T.; Levy, J. *Bull. Soc. Chim. Fr.* **1982**, 241.

(9 mL) cooled to 0 °C was added lithium aluminum hydride (72 mg, 1.77 mmol) in portions. The suspension was refluxed (3 h) and then stirred (12 h) at room temperature. The reaction was quenched following the Fieser[17] procedure, and the residue was chromatographed on silica gel (ethyl acetate) to give **14** as pale yellow crystals, mp 144–146 °C $[\alpha]^{20}_D$ −80.9° (*c* 1, MeOH) [lit.[10] mp 149–150 °C, $[\alpha]^{20}_D$ −84° (*c* 1, MeOH)].

The same product was obtained directly from **8** by using 4-chloro-1-iodobutane, in the following manner: To a stirred solution of the lithio anion (see procedure for **12**) cooled to −100 °C was added a solution of 4-chloro-1-iodobutane (340 mg, 1.56 mmol) in 5.0 mL of THF dropwise. The solution was stirred for 30 min, quenched with water, diluted with ether, and washed (3×) with water and the organic layer separated, dried (K_2CO_3), and concentrated. The hydrazine mixture, as above, was added to the residue and the MOM group removed as above. Chromatography on silica gel gave **14** in 66% yield, identical in all respects with the product obtained by hydride reduction.

(*E*)- and (*Z*)-(*S*)-(−)-Deplancheine [(*E*)- and (*Z*)-4] from 12. To a solution of **12** (370 mg, 1.30 mmol) in THF (13 mL) at 0 °C was added LDA (0.5 M, THF, 2.85 mL). The solution was stirred (1 h) and cooled in a −78 °C bath. A solution of diphenyl diselenide (450 mg, 1.4 mmol) in THF (1 mL) was added dropwise with stirring. After 30 min the dark yellow solution was warmed to 0 °C. Lithium diisopropylamide (0.5 M, THF, 2.85 mL) was added dropwise, and after 1 h the deep red solution was cooled in a −78 °C bath. An excess of acetaldehyde was distilled into the reaction flask via a cannula. The solution was stirred (1 h), quenched with water, extracted with ether, dried, and concentrated to yield a yellow oil, **15**. The oil was taken into methylene chloride (25 mL) and triethylamine (991 mg, 9.8 mmol) at 0 °C. A solution of thionyl chloride (390 mg, 3 mmol) in methylene chloride (1.0 mL) was added very slowly. The reaction was stirred (2 h), quenched with water, extracted with ether, dried, and concentrated to **16**. The latter, without further purification, was subjected to 3 N HCl in ether (1:1), stirred for 6 h, and then neutralized with 6 N KOH. Extraction with ether, washing with water, drying (Na_2SO_4), and concentration gave the lactams (*E*)- and (*Z*)-**17** as a 1.2:1 mixture. Column chromatography on silica gel (ether) afforded the pure (*Z*)- and (*E*)-**17** isomers. To the *Z* isomer of **17** (141 mg, 0.53 mmol) in dry DME (12 mL) at 0 °C was added DIBAL (1 M, toluene, 3.85 mL) dropwise. The solution was warmed to room temperature and stirred for 1 h. The reaction was quenched with methanol (12 mL) and water (1 mL) and worked up to yield an orange oil. The oil was chromatographed on silica gel (100:2 ethyl acetate–triethylamine) to afford 66 mg (35%) of (*Z*)-**4** as a white solid. Further purification was achieved by either recrystallization (ether) or sublimation [140 °C (0.2 torr)]: mp 115–117 and 165–167 °C (lit.[6c] mp 163 °C); IR (film) 3400, 3190, 2930, 2885, 2790, 2730, 1445, 1315, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (s, 1 H), 7.45 (m, 1 H), 7.28 (m, 1 H), 7.10 (m, 2 H), 5.32 (q, *J* = 6.6 Hz, 1 H), 3.81 (d, *J* = 12.6 Hz, 1 H), 3.38 (d, *J* = 11.3 Hz, 1 H), 3.03 (m, 2 H), 2.75 (m, 2 H), 2.35 (m, 2 H), 2.09 (m, 1 H), 1.66 (d, *J* = 6.7 Hz, 4 H); ^{13}C NMR ($CDCl_3$, ppm) δ 135.9, 134.7, 127.3, 121.2, 119.2, 118.6, 118.1, 110.6, 108.2, 60.0, 55.1, 53.3, 53.0, 31.1, 21.7, 13.0, 8.6; $[\alpha]^{25}_D$ −88.2° (*c* 1.02, $CHCl_3$).

The *E* isomer of **17** was treated under the same conditions as the *Z* isomer to yield 66 mg (35.4%) of (*E*)-**4** (deplancheine) as a white solid. Further purification was achieved from either recrystallization or sublimation, as above, mp 138–140 °C [lit.[5] mp 115 °C (ether), lit.[6c] 148 °C (sublimation)], $[\alpha]_D^{25}$ −51.7° ($CHCl_3$). See preparation from **22** for complete spectral details.

Ethyl (*E*)-2-(2-Bromoethyl)-2-butenoate (19a). Hydrogen bromide was passed through an ice-cooled solution of **18** (6.7 g, 0.06 mmol) in EtOH (30 mL) (HBr gas was prepared by reaction of Br_2 with tetralin). The mixture was allowed to stand at room temperature overnight and then heated at 60 °C for 1 h. The mixture was poured into brine (200 mL) and extracted with ether. The ether extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to leave an oil, which was chromatographed on silica gel with Et_2O–hexane (1:10) to give **19a** as an oil (8.0 g, 61%): IR (neat) 1700 (br), 1650 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.05 (q, *J* = 7.0 Hz, 1 H), 4.20 (q, *J* = 7.3 Hz, 2 H), 3.48 (t, *J* = 7.3 Hz, 2 H), 2.90 (t, *J* = 7.3 Hz, 2 H), 1.87 (d, *J* = 7.0 Hz, 3 H), 1.30 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$, ppm) δ 166.5, 139.9, 130.3, 60.3, 30.9, 30.0, 14.3, 14.1.

(*E*)-2-(2-Bromoethyl)-2-buten-1-ol (19b). Diisobutylaluminum hydride (1 M in hexane, 44 mL, 0.044 mmol) was added dropwise to a stirred and ice-cooled solution of **19a** (4.42 g, 0.02 mmol) in toluene (50 mL). The mixture was stirred at room temperature for 1 h, and then H_2O (30 mL) and 6 N HCl (50 mL) were added. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give **19b** as an oil (3.35 g, 93.6%): IR (neat) 3350 (br), 2940, 2880, 1005 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.68 (q, *J* = 6.8 Hz, 1 H), 4.07 (s, 2 H), 3.46 (t, *J* = 7.7 Hz, 2 H), 2.87 (s, 1 H), 2.72 (t, *J* = 7.7 Hz, 2 H), 1.68 (d, *J* = 6.8 Hz, 3 H). The oil was used for the subsequent reaction without purification.

(*E*)-2-(2-Bromoethyl)-2-buten-1-yl *tert*-Butyldimethylsilyl Ether (19c). *tert*-Butyldimethylsilyl chloride (2.0 g, 13.2 mmol) was added to a stirred mixture of **19b** (2.0 g, 11 mmol), Et_3N (2.26 g, 22 mmol), DMAP (134 mg, 1.1 mmol), and CH_2Cl_2 (25 mL). The mixture was stirred at room temperature for 1 h and was allowed to stand at room temperature overnight. The reaction mixture was concentrated in vacuo, and the residue was chromatographed on silica gel (100 g) with Et_2O–hexane (1:20, v/v) to give **19c** (2.1 g, 66%) as an oil: IR (neat) 2940, 2860, 1460, 1245, 1070, 1045, 825, 765 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 5.60 (q, *J* = 6.7 Hz, 1 H), 4.06 (s, 2 H), 3.42 (t, *J* = 7.8 Hz, 2 H), 2.66 (t, *J* = 7.8 Hz, 2 H), 1.65 (d, *J* = 6.7 Hz, 3 H), 0.90 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (270 MHz, $CDCl_3$, ppm) δ 136.7, 123.1, 67.4, 31.9, 30.8, 26.0, 18.3, 13.2, −5.3.

Alkylated Carboline 20. A solution of **8** (1.54 g, 4 mmol) in THF (35 mL) was treated with *n*-BuLi (1.35 M in hexane, 3.85 mL, 5.2 mmol) at −78 °C for 1 h, and then a solution of **19c** (1.76 g, 6 mmol) in THF (10 mL) was added dropwise at −78 °C. The mixture was stirred at the same temperature for 7 h, poured into H_2O, and extracted with Et_2O. The Et_2O extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residual oil was chromatographed on silica gel (80 g) with hexane–Et_3N (10:1, v/v) to give **20** (2.17 g, 91%) as an colorless oil: IR (neat): 2950, 2865, 1635, 1455, 1240, 1180, 820 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.49–7.41 (m, 3 H), 7.28–7.14 (m, 2 H), 5.5 (m, 1 H), 5.49 (d, *J* = 11 Hz, 1 H), 5.30 (d, *J* = 11.1 Hz, 1 H), 4.07 (s, 2 H), 3.4 (m, 3 H), 3.25 (s, 3 H), 3.2–2.5 (m, 5 H), 2.3–2.1 (m, 2 H), 2.0–1.7 (m, 3 H), 1.67 (d, *J* = 6.6 Hz, 3 H), 1.05 (s, 9 H), 0.92 (s, 9 H), 0.86 (d, *J* = 6.5 Hz, 3 H), 0.84 (d, *J* = 6.5 Hz, 3 H), 0.07 (s, 6 H); ^{13}C NMR (270 MHz, $CDCl_3$, ppm) 153.9, 139.1, 137.5, 136.7, 127.6, 121.9, 120.0, 119.5, 118.1, 109.5, 109.1, 74.3, 72.2, 71.0, 67.2, 64.9, 55.6, 32.7, 30.4, 27.6, 26.0, 25.1, 21.2, 20.5, 18.4, 17.9, 12.9, −5.3; $[\alpha]^{20}_D$ +27.0° (*c* 1.03, THF).

Alkylated Carboline 21. Acetic acid (2.5 mL) and hydrazine (5 mL) were added in this order to a stirring solution of **20** (1.9 g, 3.18 mmol) in 95% EtOH (40 mL)–H_2O (4 mL). The mixture was stirred at ambient temperature for 1 h and then concentrated in vacuo. The residue was diluted with H_2O and extracted with Et_2O. The Et_2O extract was successively washed with 10% KOH (30 mL × 2) and H_2O, dried (K_2CO_3), and concentrated in vacuo. The residue was chromatographed on silica gel (50 g) with ethyl acetate–hexane–Et_3N (5:9:1) to give **21** (1.25 g, 92%) as an oil: IR (neat) 3330, 2940, 2860, 1460, 1250, 1100, 830, 770, 735 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.49–7.39 (m, 2 H), 7.26–7.11 (m, 2 H), 5.54 (q, *J* = 6.8 Hz, 1 H), 5.40 (d, *J* = 10.9 Hz, 1 H), 5.28 (d, *J* = 10.9 Hz, 1 H), 4.10 (s, 2 H), 4.07–4.05 (m, 1 H), 3.28–3.15 (m, 2 H), 3.25 (s, 3 H), 2.75–2.72 (m, 2 H), 2.33–2.29 (m, 2 H), 1.91–1.83 (m, 3 H), 1.69 (d, *J* = 6.8 Hz), 0.91 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (270 MHz, $CDCl_3$, ppm) 139.2, 138.2, 137.5, 127.8, 121.7, 119.8, 119.7, 118.0, 109.8, 109.3, 74.2, 67.1, 55.6, 50.7, 38.9, 32.4, 26.0, 24.7, 22.8, 18.4, 13.0, −5.3; $[\alpha]^{20}_D$ +16.8° (*c* 1.03, THF).

Alkylated Carboline 22. A solution containing 900 mg of **21** in 30 mL of ether and 30 mL of THF was treated wtih 60 mL of 3 N HCl. The two-phase mixture was stirred at room temperature for 1 h and made basic (pH 12) with aqueous KOH. The mixture was stirred at ambient temperature for 30 min and allowed to stand at room temperature overnight. The organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried (K_2CO_3), and concentrated in vacuo. The residue was chromatographed

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on silica gel (25 g) with AcOEt-MeOH-Et_3N (20:1:2, v/v) to give **5** (361 mg, 64%) as crystals. Recrystallization from AcOEt-hexane gave colorless prisms: mp 142-143 °C; $[\alpha]^{20}_D$ -54.8° (*c* 1.0, $CHCl_3$), -41.1° (*c* 1.0, EtOH); IR (KBr) 3265, 3170, 2925, 1440, 1300, 985, 735 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 7.48-7.08 (m, 4 H), 5.54 (q, *J* = 6.8 Hz, 1 H), 4.07 (s, 2 H), 4.04-4.03 (m, 1 H), 3.35-3.27 (m, 2 H), 2.99-2.92 (m, 1 H), 2.74-2.70 (m, 2 H), 2.39-2.34 (m, 2 H), 2.10-2.04 (m, 1 H), 1.80-1.72 (m, 1 H), 1.65 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 140.0, 136.1, 127.9, 122.5, 121.7, 119.6, 118.2, 110.9, 109.3, 68.5, 52.9, 42.3, 33.3, 24.7, 22.8, 13.3.

Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.36; H, 8.26; N, 10.16.

(*E*)-(*S*)-(-)-Deplancheine [(*E*)-4]. A solution of 200 mg (0.74 mmol) of **22** in 5 mL of acetonitrile was treated with triphenylphosphine (291 mg, 1.11 mmol), carbon tetrachloride (228 mg, 1.48 mmol), and triethylamine (150 mg, 1.48 mmol). The mixture was stirred at room temperature for 12 h under argon and concentrated in vacuo. The residue was chromatographed on silica gel (15 g) with Et_2O-Et_3N (15:1, v/v) to give **4** (149 mg, 80%) as crystals. Recrystallization from Et_2O-hexane gave colorless crystals: mp 140.5-141.5°; $[\alpha]^{20}_D$ -52.0° (*c* 1.0, $CHCl_3$), -64.9° (*c* 1.0, EtOH); IR ($CHCl_3$) 3440, 2840-2770, 1435, 1300 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.75 (br s, 1 H), 7.48-7.08 (m, 4 H), 5.42 (q, *J* = 6.8 Hz, 1 H), 3.42-3.31 (m, 2 H), 3.1-2.98 (m, 3 H), 2.83-2.63 (m, 3 H), 2.19-2.13 (m, 1 H), 1.98 (br t, 1 H), 1.62 (d, *J* = 6.8 Hz, 3 H), 1.65-1.53 (m, 1 H); ^{13}C NMR ($CDCl_3$, ppm) 136.5, 135.0, 134.5, 127.9, 121.5, 119.6, 119.1, 118.3, 110.8, 108.7, 63.6, 60.3, 53.0, 30.4, 26.0, 21.8, 12.6.

Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.76; H, 8.12; N, 11.06.

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Micellar Catalysis of Organic Reactions. 19. Basic Hydrolysis of Carbamates in the Presence of Hydroxy-Functionalized Micelles

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A number of hydroxy-functionalized micelles were prepared, and their effects on the basic hydrolysis of a number of carbamates are compared. For reactions proceeding by the E1cB mechanism, the intermediate *p*-nitrophenyl isocyanate was trapped by the hydroxy group of the functional micelles. The efficiency of trapping by the different micelles was compared, and it was found that primary hydroxyl groups were more active than secondary ones. Furthermore, hydroxy groups bonded to the ethyl or propyl groups of detergent molecules **7** and **9** were more effective than those attached to the cetyl chain of **8**. The effects of the various micelles on the rate of E1cB hydrolysis and on $B_{Ac}2$ hydrolysis of carbamates and on the decarboxylation of aryl carbamate ions in basic solution were also compared.

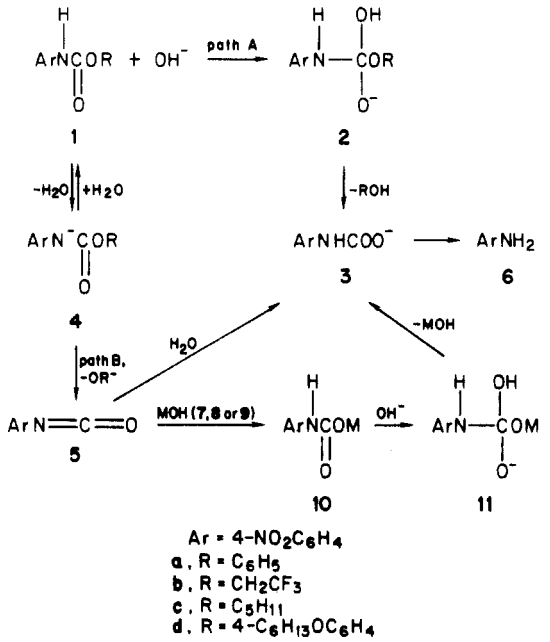
The basic hydrolysis of carbamates is of current interest.[1-5] One reason for this interest is the competition between the E1cB (path B) and $B_{Ac}2$ (path A) mechanisms for the basic hydrolysis of carbamates (Scheme I).

Good evidence for the occurrence of the E1cB mechanism in the basic hydrolysis of the phenyl and 2,2,2-trifluoroethyl compounds **1a,b** was obtained[6] by trapping the intermediate *p*-nitrophenyl isocyanate (**5**) with the hydroxy group of the functional micelle cetyl(2-hydroxyethyl)dimethylammonium bromide (chedab) (**7**). Since this intermediate **5** is not formed on path A, this result confirms that the mechanism operating for the hydrolysis of compounds **1a,b** is the E1cB mechanism (path B). The micellar carbamate **10** thus formed, subsequently decomposed slowly via the $B_{Ac}2$ mechanism (**10** → **11** → **3** → **6**).

For the *n*-pentyl compound **1c**, hydrolysis occurred by the $B_{Ac}2$ mechanism (**1c** → **2c** → **3** → **6**), but the catalysis provided by the functional micelles of chedab and by nonfunctional micelles of cetyltrimethylammonium bromide (ctab) was very similar.[6]

It is now of interest to vary the nature of the hydroxy group in the functional micelle (e.g., primary vs. secondary)

Scheme I



and also to vary the position at which the hydroxy group is bonded to the micelle. In this paper we report the preparation of two other hydroxy-functionalized micelles: 2-hydroxycetyltrimethylammonium bromide (**8**) and cetyl(2-hydroxy-1-propyl)dimethylammonium bromide (**9**).

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