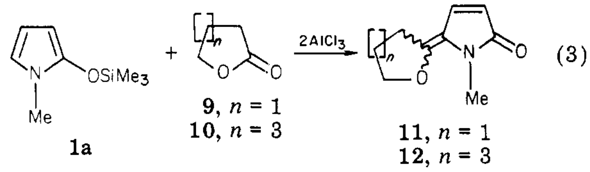
made to separate these compounds by TLC. With acrolein and 2-cyclohexenone, the 1,4-addition products **7a,b** and **8a,b** were obtained in good to high yields (38–83%). In all cases the substitution reactions were regiospecific in that only C-5 was attacked, no reaction being seen at C-3.

Whereas $SnCl_4$ proved to be the most effective Lewis acid catalyst in the functionalization of **1a** and **1b** with all the carbonyl electrophiles, the corresponding reaction with saturated lactones was successful only with **1a** in the presence of 2 equiv of $AlCl_3$. Moreover only γ-butyrolactone (**9**) and ϵ-caprolactone (**10**) were found to react to give, after a hydrolytic workup, compounds **11** and **12** (eq 3).

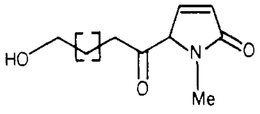


1a

9, $n = 1$
10, $n = 3$

11, $n = 1$
12, $n = 3$

Most likely compounds **11** and **12** were generated through compound **13** which undergoes intramolecular cyclization under the acidic workup conditions.



13

The regiospecific electrophilic substitution at position 5 of 2(5*H*)-pyrrolone and 2(5*H*)-thiophenone ring systems starting from the corresponding siloxy heterocycles appears synthetically attractive, being somewhat simpler than the methods previously reported in the literature for compounds listed in Table I[4-6] and much more general in that it can be extended to a much wider range of electrophiles.

The general scope and the limits of this reaction are currently being considered.

Experimental Section

Boiling points were uncorrected. ^1H NMR spectra were obtained on a Perkin-Elmer R-32 90-MHz spectrometer; chemical shifts are reported in δ units downfield from internal Me_4Si. IR spectra were recordered in CCl_4 or as a liquid film with NaCl cells on a Perkin-Elmer 283 spectrophotometer; mass spectra and GC/MS were determined on a Varian Matt 111 instrument equipped with an OV-101 5% column. Preparative TLC were carried out on E. Merck silica gel F plates and visualized by ultraviolet lights; column chromatography was carried out with a 25-cm column filled with silica gel containing $CaSO_4$ or with a Jobin Yvon Chromatospac preparative column with silica gel (H-60, 15 μm). Microanalysis was performed with a Perkin-Elmer 240 C analyzer. Compounds **1a** and **1b** were prepared according to Baker[7] and Hawkins,[8] respectively; the silylating reagents are commercially available from Aldrich Chemical Co. and Fluka AG chemicals.

1-Methyl-2-(trimethylsiloxy)pyrrole (1a). To a cooled solution (0 °C) of 1.45 g (10 mmol) of Me_3SiDEA in dry Et_2O (2 mL) under nitrogen atmosphere and with magnetic stirring was added a solution of 0.97 g (10 mmol) of **2a** dropwise. The reaction mixture was allowed to warm to room temperature, and the conversion was judged, by ^1H NMR and GC analyses, to be complete after 12 h. Evaporation of the crude reaction mixture followed by vacuum distillation afforded **1a**: 1.18 g (70% yield); bp 64–65 °C (7.5 mmHg); IR (CCl_4) 3100, 2960, 1250, 920, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H, Si $(CH_3)_3$), 3.41 (s, 3 H, NCH_3), 5.25 (m, 1 H, heterocyclic ring), 5.93 (m, 1 H, heterocyclic ring), 6.17 (m, 1 H, heterocyclic ring). Anal. Calcd for $C_8H_{15}NOSi$: C, 56.80; H, 8.87; N, 8.28. Found: C, 56.62; H, 8.89; N, 8.27.

2-(Trimethylsiloxy)thiophene (1b). To a cooled solution (−78 °C) of 5.00 g (50 mmol) of **2b** and 10.8 g (100 mmol) of Me_3SiCl in dry Et_2O (25 mL) under nitrogen atmosphere and with mechanical stirring was added a solution of 7.25 g (50 mmol) of Me_3SiDEA in 25 mL of dry Et_2O dropwise. After 4 h at −78 °C, GC analysis of the reaction mixture again revealed the presence of **2b** that was completely converted into **1b** by addition of 1.08 g (7 mmol) of Me_3SiDEA. Et_2NH–HCl was filtered off and the solvent evaporated to give, after vacuum distillation, **1b**: 5.59 g (65% yield); bp 50–52 °C (0.75 mmHg); IR (CCl_4) 3080, 2960, 1570, 1250, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.38 (s, 9 H, $Si(CH_3)_3$), 6.15 (m, 1 H, heterocyclic ring), 6.55 (m, 1 H, heterocyclic ring), 6.70 (m, 1 H, heterocyclic ring). Anal. Calcd for $C_7H_{12}OSSi$: C, 48.82; H, 6.98. Found: C, 48.68; H, 6.99.

General Procedure for the Preparation of 3a and 3b. An equimolar mixture of $PhSSiMe_3$ and **2a,b** was maintained at room temperature under nitrogen and with magnetic stirring for 10 h. Compounds **1a** and **1b** were removed under vacuum, affording crude **3a,b** which were further purified by fractional distillation.

3a: bp 75 °C (0.03 mmHg); 60% yield; IR (liquid film) ν_{CO} 1695 cm^{-1}; ^1H NMR (CCl_4) δ 2.75 (s, 3 H, NCH_3), 3.2–3.4 (m, 2 H, CO–CH_2), 3.7–3.9 (m, 2 H, N–CH_2), 3.9–4.2 (m, 1 H, CH–S), 7.40 (m, aromatics); MS, *m/e* 207 (M^+, base). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.77; H, 6.27; N, 6.75. Found: C, 63.96; H, 6.26; N, 6.73.

3b: bp 113–115 °C (0.11 mmHg); 45% yield; IR (liquid film) ν_{CO} 1705 cm^{-1}. ^1H NMR δ 2.3–3.0 (m, 2 H, CO–CH_2), 3.2–3.7 (m, 2 H, S–CH_2), 3.7–4.1 (m, 1 H, S–CH), 7.45 (m, 5 H, aromatics); MS, *m/e* 210 (M^+, base). Anal. Calcd for $C_{10}H_{10}OS_2$: C, 57.13; H, 4.75. Found: C, 57.29; H, 4.74.

General Procedure for the Regioselective Functionalization of the Heterocyclic Rings 1a and 1b with Electrophiles. To a cooled (−78 °C) solution of 3 mmol of **1a** or **1b** and of the appropriate electrophile (3 mmol) in dry CH_2Cl_2 (5 mL) under an argon atmosphere and with magnetic stirring was rapidly added the required amount of Lewis acid catalyst (see Table I). The hydrolytic workup with HCl 0.1 N solution followed by evaporation of the organic layer afforded crude substituted unsaturated lactams and thiolactones **4–12**, which were obtained as colorless or yellow oils after purification by PTLC or column chromatography on silica gel (see Table I). Only compounds **4a** and **4b** slowly solidified on standing to waxy materials.

Registry No. **1a**, 87884-52-4; **1b**, 83043-44-1; **2a**, 13950-21-5; **2b**, 3354-32-3; **3a**, 87884-53-5; **3b**, 87884-54-6; (*E*)-**4a**, 87884-55-7; (*Z*)-**4a**, 87884-56-8; **4b**, 13755-25-4; (*E*)-**5a**, 87884-57-9; (*Z*)-**5a**, 87884-58-0; **5b**, 6542-68-3; **6a**, 78210-72-7; **6b**, 87884-59-1; **7a**, 87884-60-4; **7b**, 87884-61-5; **8a**, 87884-62-6; **8b**, 87884-63-7; **9**, 96-48-0; **10**, 502-44-3; **11**, 87884-64-8; **12**, 87884-65-9; Me_3SiDEA, 996-50-9; Me_3SiCl, 75-77-4; $PhSSiMe_3$, 4551-15-9; $Me_3SiSSiMe_3$, 3385-94-2; Me_3SiSMe, 3908-55-2; $SnCl_4$, 7646-78-8; $AlCl_3$, 7446-70-0; benzaldehyde, 100-52-7; butyraldehyde, 123-72-8; acetone, 67-64-1; acrolein, 107-02-8; 2-cyclohexenenone, 930-68-7.

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A Short Synthesis of 4,5-Methanochrysene and 6-Oxo-7-oxabenzo[*a*]pyrene,[1] Two Benzo[*a*]pyrene Analogues

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Methylated polynuclear aromatic hydrocarbons are often more carcinogenic than the parent derivatives. It is known that the bay region methylated 5-methylchrysene (1) is a

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(1) Conventional numbering system used for benzo[*a*]pyrene derivatives. See structure 5.

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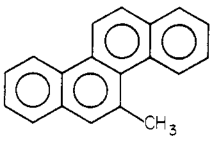
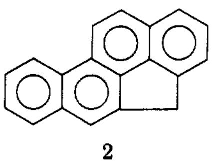
highly active carcinogen, while chrysene and other monomethylchrysenes are only weakly active.[2,3] Structure-activity studies have shown that position C-4 in chrysene cannot be substituted for metabolism to occur to the dihydrodiol epoxide, which is the ultimate mutagen and carcinogen responsible for the toxicological activity of these compounds.[4] We were interested in the toxicological properties of 4,5-methanochrysene (**2**)[5] in which one of the two "bay regions"[6] is blocked from metabolic activation in order to assess the steric vs. electronic effects of alkyl substitution on the metabolic activation of these bay region PAHs. Furthermore, 4,5-methanochrysene (**2**) can be considered as a norbenzo[*a*]pyrene and as such may be expected to exhibit similar potent carcinogenic activity.[6] In light of current interest in cyclopentene fused PAHs,[7,8] we report in this paper a short synthesis of **2** and lactone **5**, the latter formed from an unusual intramolecular photochemical cyclization of an arenecarboxylic acid and also of interest in toxicology.[9]



1

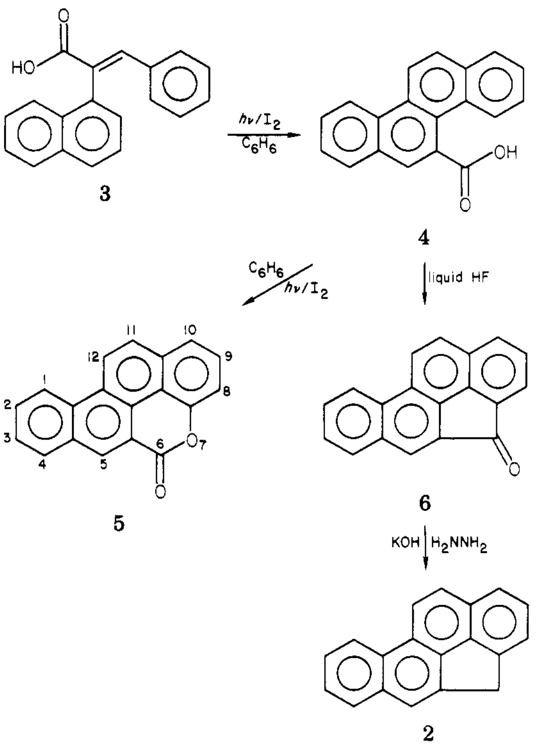


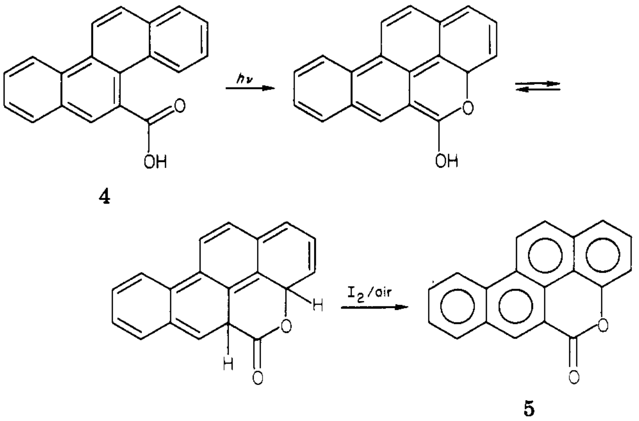
2

The substrate used for this synthesis was 5-chrysenecarboxylic acid (**4**), which was obtained by a modified procedure as described by Amin.[9] The key step involved the oxidative photocyclization of stilbenecarboxylic acid **3**. Although the desired chrysenecarboxylic acid (**4**) was formed as the major product (58%), a small amount of lactone **5** was formed, the amount of which was dependent on the irradiation time. In order to ascertain that lactone **5** was formed as a secondary photoproduct, the irradiation of **4** was carried out under identical conditions and found to be slowly transformed to lactone **5**. The structure of lactone **5** was assigned by comparison of its spectral data with those of an authentic sample.[13]

Cyclization of acid **4** in liquid HF gave the pentacyclic ketone **6** in 65%. A modified Wolff–Kishner reduction[10] of this ketone gave 4,5-methanochrysene (**2**) in 60% yield. The UV spectrum of **2** was found to be similar to that of chrysene.

The formation of lactone **5** from carboxylic acid **4** involves an unusual intramolecular photoaddition of arenecarboxylic acid. Such transformation can be rationalized in terms of a 6π electrocyclization involving the carbonyl group followed by oxidation of the dihydroaromatic lactone. Electrocyclization (6π) of unsaturated ketones have been reported under photolytic conditions.[11] The mutagenic studies of **5** has been reported and found to parallel that of benzo[*a*]pyrene.[9] The mutagenic activity of the methanochrysenes **2** and **6** are currently being investigated in these laboratories.[14]





Experimental Section

Melting points were determined on a Reichert melting point apparatus and were uncorrected. All ^1H NMR spectra were run on compounds in $CDCl_3$ solutions with tetramethylsilane as the internal standard, using either a Varian EM 360 or Bruker WH-400 instrument (Southwestern Ontario Regional High-Field NMR Centre, University of Guelph). IR spectra were recorded on a Unicam SP 1000 instrument. Mass spectra were obtained from a V. G. Micromass 16F spectrometer at 70 eV. 2-(1-Naphthyl)-3-phenylpropenoic acid was prepared according to the method described by Amin.[9] Photocyclization to chrysene-5-carboxylic acid was carried out by a modified literature method,[9] which is described below.

Chrysene-5-carboxylic Acid (4). A solution of 400 mg of 2-(1-naphthyl)-3-phenylpropenoic acid (**3**) and 17.5 mg I_2 in 500 mL of benzene (BDH crystallizable, acid washed, dried over $LiAlH_4$, and distilled) was irradiated for 3 h with a 450-W high-pressure Hg lamp (Hanovia Corp.) fitted with a Vycor filter. Dry

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(13) We thank Dr. Amin of the American Health Foundation, Valhalla, NY, for providing us with authentic lactone **5**.

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air was bubbled through the solution during irradiation. The solvent was evaporated. The orange oil solidified on standing. This was dissolved in 50 mL of a saturated Na_2CO_3 solution and then extracted with ether (3 × 30 mL). The Na_2CO_3 extracts were combined and acidified with concentrated HCl. This was back-extracted three times with 10 mL of ether and the ether extract was washed with water, dried over $MgSO_4$, and evaporated to give 4 (58%), mp 212–224 °C (lit.[12] mp 225–226 °C).

The ether extracts containing neutrals was washed with water, dried, and evaporated. The residue was chromatographed on a short alumina column with benzene/ether to give 5 (25%): mp 215–220 °C (lit.[9] mp 225–226 °C); MS, *m/e* 270 (M^+, 100), 242 (16).

Irradiation of Chrysene-5-carboxylic Acid (4). Preparation of Lactone 5. A solution of 70 mg of 4 and 4 mg of I_2 in 250 mL of benzene was irradiated as described above for 24 h. Evaporation of benzene gave a residue, which was applied on a thin-layer chromatography plate (benzene eluant), giving 35% of lactone 5 identical in all respects with a sample prepared above.

Pentacyclic Ketone 6. A 500-mg sample of chrysene-5-carboxylic acid (4) was placed in a Teflon container and cooled to −75 °C. Liquid HF was then added from an inverted gas cylinder with a direct inlet to the reaction vessel. The solution was stirred at −75 °C for 1 h and then placed in an ice bath and stirred overnight while slowly warming to room temperature, and the HF then was allowed to evaporate. The residue was dissolved in THF, adsorbed on silica gel, and evaporated to dryness. The adsorbed compound on silica gel was placed on a short silica gel column and eluted with benzene. A yellow solid 6 was obtained (65% yield), which was recrystallized from 95% ethanol: mp 205–207 °C; IR 1708 (C=O) cm^{-1}; NMR 8.68 (d 1 H), 8.52 (d, 1 H), 8.34 (s, 1 H), 8.22 (d, 1 H), 8.19 (d, 1 H), 8.12 (d, 1 H), 8.07 (d, 1 H), 7.95 (t, 1 H), 7.80–7.87 (m, 2 H); MS, *m/e* 254 (M^+, 100), 226 (20), 224 (30).

4,5-Methanochrysene (2). A solution of 100 mg of pentacyclic ketone 6, 100 mg of KOH, and 100 mg of hydrazine hydrate in 10 mL of ethanediol was heated and stirred under nitrogen at 175 °C overnight. The suspension was allowed to cool, poured into 30 mL of H_2O, and extracted three times with 25 mL of $CHCl_3$. The $CHCl_3$ extracts were combined, washed with water, and evaporated. The residue was applied on a preparative silica gel (1-mm thickness) thin-layer chromatography plate and eluted with hexane. A white crystalline material (2) was obtained (60% yield): mp 174–176 °C (lit.[5] mp 171–173 °C); IR (KBr) 1403, 822, 767, 750 cm^{-1}; NMR 8.65 (d, 1 H), 8.49 (d, 1 H), 8.04 (d, 1 H), 7.98 (d, 1 H), 7.93 (s, 1 H), 7.86 (t, 1 H), 7.5–7.7 (m, 4 H), 4.47 (s, 2 H); MS *m/e* 240 (M^+, 100), 239 (70); UV (EtOH, 95%) max 327, 313, 302, 267, 261, 218 nm.

Acknowledgment. This work is supported by grants from the Ministry of Environment Province of Ontario and by the Natural Science and Engineering Research Council of Canada. We thank the Southwestern Ontario Regional NMR Centre for running the 400-MHz spectra.

Registry No. 2, 202-98-2; 3, 71432-05-8; 5, 71432-00-3; 6, 86853-91-0; 4, 68723-48-8.

Asymmetric Reduction of Aliphatic Ketones with the Reagent Prepared from (*S*)-(−)-2-Amino-3-methyl-1,1-diphenylbutan-1-ol and Borane

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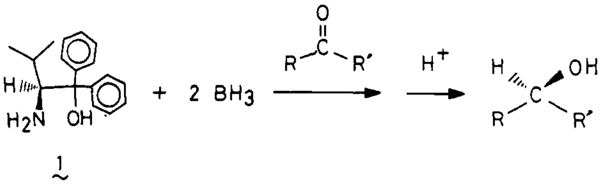
In asymmetric synthesis, both high stereoselectivity and practical usefulness of the reagent have been important subjects. From this point of view, the use of chirally modified metal hydrides for the asymmetric reduction of prochiral ketones has continued to be actively studied. The most widely studied examples are those using lithium aluminum hydride (LAH) modified by optically active alcohols and amines, some of which give substantial stereoselectivities in reductions of *α,β*-unsaturated ketones such as acylophenone,[1-4] enones,[5,6] and ynones.[7-9] Only limited success, however, has been achieved for aliphatic ketones. For example, the chiral binaphthyl/LAH[4] and chiral diamine/LAH,[3] which are highly effective for aromatic ketones, reduced 2-octanone in only 24% ee and 26% ee, respectively. Besides chirally modified LAH, (bornyloxy)aluminum dichloride,[10] dipinanylborane,[11] and lithium trialkylborohydride (Li(HB-IPC-9-BBN))[12] were examined for the asymmetric reduction of aliphatic ketones to give optical yields below 50% ee. For example, 3,3-dimethyl-2-butanone was tested with these reagents to give the alcohol with 28% ee at most to a low of 3% ee.

Scheme I



Very recently, lithium trialkylborohydride, NB-Enantride (Aldrich), which is prepared by hydroboration of 6,6-dimethyl-2-[2-(phenylmethoxy)ethyl]bicyclo[3.1.1]hept-2-ene(nopol benzyl ether) with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by treatment with *tert*-butyllithium, has been shown to be a very effective chiral reducing agent for the reduction of straight-chain aliphatic ketones.[13] Asymmetric reduction of 2-octanone with NB-Enantride at −78 °C gave (*S*)-2-octanol in 79% ee, which is the highest value so far reported for aliphatic secondary alcohols. However, NB-Enantride was not effective for 3,3-dimethyl-2-butanone, which has a larger steric difference in the alkyl groups on both sides of the carbonyl group.

We have observed that the reagent prepared from (*S*)-(−)-2-amino-3-methyl-1,1-diphenylbutan-1-ol (1) and borane can be successfully used in asymmetric reduction of aromatic ketones to give the (*R*)-benzyl alcohols in 94–100% ee.[14] These results encourage us to apply the reagent to asymmetric reduction of aliphatic ketones. We now disclose our finding that the reduction of aliphatic ketones with the reagent prepared from 1 and borane

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