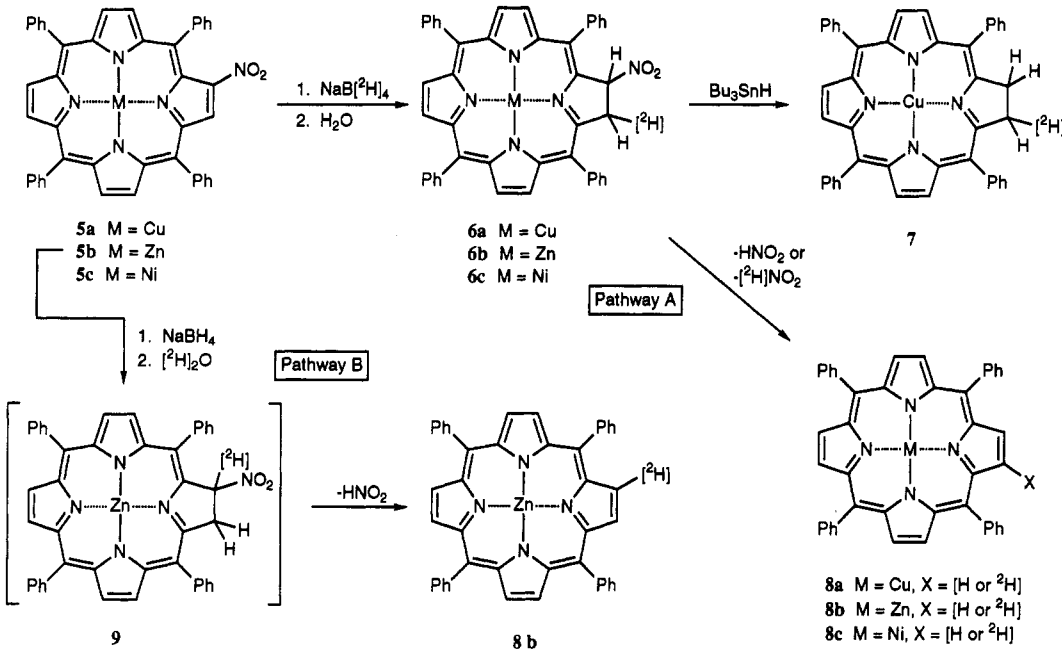
Scheme II



macrocycle. Appropriate use of unlabeled reagent or the deuteriated analogs of $NaBH_4$, H_2O, and Bu_3SnH would allow the parent chlorin, 2,3-dihydro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin (**3**), to be prepared as the [2-$^2H_1$], [2,2-$^2H_2$], [2,3-$^2H_2$], or the [2,2,3-$^2H_3$] derivative as desired.

The procedure was also amenable to the preparation of metallochlorins from the corresponding metallo-2-nitroporphyrins and once again allowed the regiospecific introduction of a deuterium atom into the reduced pyrrole ring of the chlorin (Scheme II). In this case, reactions of (2-nitro-5,10,15,20-tetraphenylporphyrinato)copper(II),[19,20] -zinc(II),[20,21] and -nickel(II) (**5a-c**) were investigated, the nickel porphyrin **5c** being obtained in 73% yield by nitration of (5,10,15,20-tetraphenylporphyrinato)nickel(II) using nitrogen dioxide.[20]

Thus, reaction of a solution of (2-nitro-5,10,15,20-tetraphenylporphyrinato)copper(II) (**5a**) in Me_2SO with sodium borodeuteride afforded (2,3-dihydro-2-nitro-5,10,15,20-tetraphenyl[3-$^2H_1$]porphyrinato)copper(II) (**6a**) in quantitative yield (Scheme II, pathway A). The blue-green nitrochlorin **6b** had a distinctive chlorin-like visible spectrum[3,18] and nitro stretch (ν_{max} 1550) in the infrared spectrum; however, no parent ion was able to be detected in the mass spectrum because of facile thermal elimination of nitrous acid. Subsequent reductive denitration with tributyltin hydride and AIBN gave (2,3-dihydro-5,10,15,20-tetraphenyl[2-$^2H_1$]porphyrinato)copper(II)[22] (**7**) in 76% yield with only a trace of the corresponding elimination product **8a**.

Deliberate promotion of nitrous acid elimination from deuterium labeled metallonitrochlorins provided access to regiospecifically deuterium labeled porphyrins. Both heat and chromatography of the nitrochlorin **6a** over silica promoted the elimination of nitrous acid and afforded (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)copper(II) (**8a**) (67% yield overall from **5a**, 53 atom % deuterium). Similar treatment of (2-nitro-5,10,15,20-tetraphenylporphyrinato)zinc(II) (**5b**) with borodeuteride followed by chromatography afforded (5,10,15,20-tetraphenyl[2-^{2}H]-porphyrinato)zinc(II) (**8b**) (51% yield, 47 atom % deuterium). Likewise, reaction of a suspension of (2-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**5c**) with borodeuteride and subsequent chromatography gave (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)nickel(II) (**8c**) (20% yield, 55 atom % deuterium) together with recovered starting nitroporphyrin **5c** (75%), the low conversion in this case being due to the low solubility of the starting porphyrin in the reaction mixture.

In these metalloporphyrin cases, the observation of approximately 50% deuterium incorporation is consistent with nonselective protonation of an intermediate nitronate ion to give an equimolar mixture of diastereomeric 2,3-dihydro-2-nitro-[3-$^2H_1$]porphyrins **6a-c**. Elimination of nitrous or deuterionitrous acid from the appropriate diastereomer will then give rise to the parent porphyrin **8a-c** with 50 atom % deuterium.

Use of a different combination of deuterium labeling in the reagents allowed regiospecific replacement of the nitro group of (2-nitro-5,10,15,20-tetraphenylporphyrinato)zinc(II) (**5b**) by deuterium to give (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)zinc(II) (**8b**) (>98 atom % deuterium) (Scheme II, pathway B). This was accomplished by performing the reaction with borohydride and quenching the reaction with D_2O; elimination of nitrous acid from the intermediate 2-deuterio-2-nitro-2,3-dihydroporphyrin **9**, facilitated by absorption onto silica, then gave the 2-deuterioporphyrin (**8b**).

While the reaction of 2-nitroporphyrin with borodeuteride (Scheme II, pathway A) provided a simple and convenient method for the partial (~50 atom %) incorporation of a deuterium atom into the β-pyrrolic site adjacent to that previously occupied by the nitro group,

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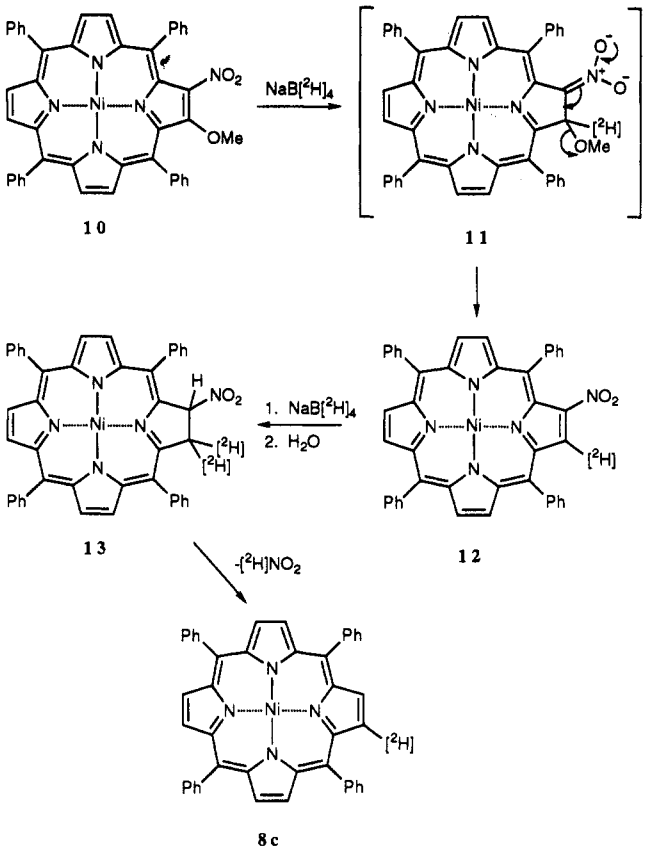
(21) Shine, H. J.; Padilla, A. G.; Wu, S.-M. *J. Org. Chem.* **1979**, *44*, 4069–4075.
(22) Several syntheses of unlabeled material have been reported: Egorova, G. D.; Mashenkov, V. A.; Solov'ev, K. N.; Yushkevich, N. A. *Zh. Prikl. Spekrosk.* **1973**, *19*, 838–842 (*Chem. Abstr.* **1974**, *80*, 65214u). Anderson, L. A.; Loehr, T. M.; Sotiriou, C.; Wu, W.; Chang, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 2908–2916. Lahiri, G. K.; Summers, J. S.; Stolzenberg, A. M. *Inorg. Chem.* **1991**, *30*, 5049–5052.

Scheme III



10 11 13 12 8c

a method to fully deuteriate this site was required. We reasoned that this could be achieved if a leaving group other than hydrido was positioned at the site required to be deuteriated. This was accomplished by reaction of borodeuteride with 2-methoxy-3-nitroporphyrin **10** (Scheme III); the synthesis of **10** was achieved by treatment of **5c** with methoxide.[15]

The reaction of borodeuteride ion with (2-methoxy-3-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**10**) was found to proceed with rapid substitution of a deuteron for the methoxyl to give the corresponding metallo-2-nitro-[3-^{2}H]porphyrin **12** that then underwent a slower second nucleophilic attack to give the metallo-2,3-dihydro-2-nitro-[2,2-$^2H_2$]porphyrin **13**. As was observed with the monodeuteriated nitrochlorins **6**, elimination of deuterionitrous acid then gave [2-^{2}H]porphyrin **8c**. Chromatography of the products of a reaction mixture quenched after 15 min by addition of water afforded nickel(II) [2-^{2}H]porphyrin **8c** (>98 atom % deuterium, 36%) and nickel(II) 2-nitro-[3-^{2}H]porphyrin **12** (>98 atom % deuterium, 55%). Compound **12** has proved very valuable in mechanistic studies of other reactions of 2-nitroporphyrins; these studies will be reported separately.

The reactivity of the borohydride nucleophile toward 2-nitroporphyrins parallels that of alkoxide nucleophiles[15] which also give conjugate addition. In contrast, the "soft" α-benzaldoximate nucleophile gives ipso substitution with nitroporphyrins,[23] as do reactions with thiolate nucleophiles.[24] While both the copper(II) and nickel(II) 2-nitroporphyrins **5a** and **5c** show all of these reactions, the relatively electron-rich zinc(II) 2-nitro-5,10,15,20-tetraphenylporphyrin (**5b**) only reacts with borohydride.

The facility of this conjugate addition on the periphery of an aromatic molecule is due to the nature of porphyrin aromaticity. The β–β bond bearing the nitro substituent can behave as a nitroene system without disrupting the aromaticity of the macrocycle. In the case of the free base **1**, the tautomer 2-nitro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin, in which there is an isolated nitroene system, is heavily favored in solution at tautomeric equilibrium.

Conclusion

The two step reduction of the easily accessible 2-nitro-5,10,15,20-tetraphenylporphyrin[20] to the corresponding chlorin via borohydride addition and reductive radical denitration provides a facile, high-yielding procedure which is both regiospecific and amenable to use in the presence of other reducible side chains, e.g. vinyl groups. Furthermore, this procedure is clearly adaptable to the preparation of chlorins with one to four deuterium (or tritium) atoms in the chlorin ring by a combination of choice of starting material (nitroporphyrin or 2-methoxy-3-nitroporphyrin) and/or the use of a D_2O quench and/or tributyltin deuteride at the appropriate stage in the sequence.

The regioselective β-deuteriation of a porphyrin ring at a site vicinal to that previously occupied by a nitro group is readily achieved with 50% deuterium incorporation by the reaction of borodeuteride ion with a 2-nitroporphyrin, an H_2O quench, followed by elimination of nitrous acid or deuterionitrous acid. Regioselective replacement of the nitro group by deuterium is readily achieved with 100% deuterium incorporation by the reaction of borohydride ion with a 2-nitroporphyrin and a D_2O quench, followed by elimination of nitrous acid. This deuteriation methodology complements the existing procedure for the deuteriation of the porphyrin ring involving *ipso* replacement of a nitro group with deuterium via the intermediacy of an (arylthio)porphyrin.[25]

This work is a further illustration of that 2-nitroporphyrins are versatile starting materials for introduction of other functionality to the porphyrin periphery.[15,23,25-29]

Experimental Section

Melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 221 spectrometer or a Perkin-Elmer 710B spectrometer. Electronic spectra were recorded on a Hitachi 150-20 spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker WM 400 spectrometer (400 MHz), with tetramethylsilane as internal standard. Mass spectra were recorded at 70 eV on an A.E.I. MS 902 spectrometer. Deuterium content of deuteriated compounds was determined from their mass spectrum and checked by computer simulation of the spectrum. Microanalyses were performed by the Australian Mineral Development Laboratory, Melbourne, Australia.

Column chromatography was routinely carried out using the flash chromatography technique on Merck silica gel type 9385

(23) Crossley, M. J.; King, L. G.; Pyke, S. M. *Tetrahedron* **1987**, *43*, 4569–4577.
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(27) Crossley, M. J.; Burn, P. L. *J. Chem. Soc., Chem. Commun.* **1987**, 39–40.
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(29) Crossley, M. J.; Gosper, J. J.; King, L. G. *Tetrahedron Lett.* **1988**, *29*, 1597–1600.

(230-400 mesh). All commercial solvents were redistilled prior to use. Light petroleum refers to the petroleum fraction of bp 60–80 °C. Where solvent mixtures are used, the proportions are given by volume.

2,3-Dihydro-2-nitro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin (2a). A solution of 2-nitro-5,10,15,20-tetraphenylporphyrin[20,21,28] (1) (49 mg, 0.074 mmol) in Me_2SO (25 mL) was stirred with sodium borohydride (7 mg, 0.18 mmol) for 15 min. The mixture was then diluted with dichloromethane (50 mL), washed with water (5 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and the solvent was removed by rotary evaporation at room temperature to afford chlorin **2a** as a brown solid in quantitative yield: mp >350 °C (decomposes with elimination of nitrous acid >50 °C); IR ν_{max} (Nujol) 3350 br (NH), 1545 cm^{-1} (unconjugated NO_2); UV and vis λ_{max} ($CHCl_3$) 367, 407sh, 418, 484sh, 517, 546, 591, 644 nm (log ϵ 4.55, 5.19, 5.32, 3.64, 4.17, 4.14, 3.84, 4.35); ^1H NMR δ (CD_2Cl_2) −1.84 (1 H, br s, interior NH), −1.77 (1 H, br s, interior NH), 4.55 (1 H, dd, $J_{2\alpha,3\beta}$ = 2.1 Hz, $J_{3\alpha,3\beta}$ = 18.4 Hz, H-3β), 4.76 (1 H, dd, $J_{2\alpha,3\alpha}$ = 9.6 Hz, $J_{3\alpha,3\beta}$ = 18.4 Hz, H-3α), 7.24 (1 H, dd, $J_{2\alpha,3\beta}$ = 2.1 Hz, $J_{2\alpha,3\alpha}$ = 9.6 Hz, H-2α), 7.61-7.83 (14 H, m, H_m and H_p of 4 phenyls and H_o of 1 phenyl), 8.01–8.11 (4 H, m, H_o of 2 phenyls), 8.13–8.24 (2 H, m, H_o of 1 phenyl), 8.30 and 8.68 (2 H, d of ABq, $^4J_{NH-H}$ = 1.0 Hz, $J_{7,8}$ = 4.8 Hz, H-7,8), 8.38 and 8.72 (2 H, d of ABq, $^4J_{NH-H}$ = 1.0 Hz, $J_{17,18}$ = 4.7 Hz, H-17,18), 8.48 and 8.51 (2 H, ABq, J = 4.8 Hz, H-12,13); MS m/z 614 (M − HNO_2, 100%). Attempts to prepare a sample for combustion analysis by an additional chromatography step or by recrystallization resulted in contamination of the product with 5,10,15,20-tetraphenylporphyrin (4) from a facile elimination of nitrous acid.

2,3-Dihydro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin (3). To refluxing dry benzene (25 mL) under nitrogen were sequentially added AIBN (130 mg, 0.79 mmol), tributyltin hydride (1 mL), and a solution of 2,3-dihydro-2-nitro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin (**2a**), prepared by the method described above from 2-nitro-5,10,15,20-tetraphenylporphyrin (1) (49 mg, 0.074 mmol) in dry benzene (8 mL). The mixture was refluxed under nitrogen for 1.5 h and allowed to cool, and the solvent was removed by rotary evaporation. The residue was triturated with light petroleum (4 × 100 mL), and the soluble fractions were filtered through a silica column (6 cm diameter, 100 g) under vacuum. The process was repeated using successively more polar mixtures of dichloromethane/light petroleum (1:9, 100 mL), (1:4, 100 mL), (3:7, 100 mL) and (2:3, 250 mL). The first and major brown band to be eluted from the column was collected and evaporated to dryness to yield 2,3-dihyro-5,10,15,20-tetraphenyl-22*H*,24*H*-porphyrin (**3**) (37 mg, 81% from the nitroporphyrin **2a**): mp >350 °C; IR ν_{max} (nujol) 3300 br (NH), 1560 s cm^{-1}; UV and vis λ_{max} ($CHCl_3$) 372, 407sh, 420, 484, 520, 547, 598, 652 nm (log ϵ 4.49, 5.10, 5.29, 3.60, 4.14, 3.98, 3.72, 4.46) [lit.[18] λ_{max} (benzene) 419, 517, 542, 598, 652 nm (log ϵ 5.28, 4.20, 4.08, 3.79, 4.62)]; ^1H NMR δ ($CDCl_3$) −1.44 (2 H, br s, NH), 4.15 (4 H, s, 2 × CH_2), 7.64–7.71 (12 H, m, H_m and H_p), 7.84–7.90 (4 H, m, H_o at C-5,20), 8.08–8.13 (4 H, m, H_o at C-10,15), 8.17 and 8.56 (4 H, br ABq, J = 5 Hz, H-7,8,17,18), 8.41 (2 H, s, H-12,13); MS m/z 618 (15), 617 (52), 616 (M^+, 100%), 615 (30), 614 (M − 2H, 38).

(2,3-Dihydro-2-nitro-5,10,15,20-tetraphenyl[3-$^2H_1$]-porphyrinato)copper(II) (6a) and (5,10,15,20-tetraphenyl-[2-^{2}H]porphyrinato)copper(II) (8a). A solution of (2-nitro-5,10,15,20-tetraphenylporphyrinato)copper(II)[19,20] (**5a**) (97 mg, 0.13 mmol) in dry, distilled Me_2SO (50 mL) was stirred under nitrogen with sodium borodeuteride (50 mg, 1.2 mmol) for 20 min. The mixture was diluted with dichloromethane (100 mL), washed with water (6 × 200 mL), dried over anhydrous Na_2SO_4, and filtered, and the solvent was removed by rotary evaporation at room temperature to afford (2,3-dihydro-2-nitro-5,10,15,20-tetraphenyl[3-$^2H_1$]porphyrinato)copper(II) (**6a**) as a blue-green solid in quantitative yield: mp >350 °C (decomposes >50 °C); IR ν_{max} (Nujol) 1600, 1550 (NO_2), 1340 cm^{-1} (NO_2); UV and vis λ_{max} ($CHCl_3$) 414, 474sh, 508, 540, 574, 608 nm (log ϵ 5.42, 3.46, 3.64, 3.83, 3.89, 4.37); MS m/z 679 (25%), 678 (56), 677 (75), 676 (M-HNO_2, 100), 675 (M − [^{2}H]NO_2, 63).

Chromatography of crude **6a** on a silica column (4 cm diameter, 200 g) eluted with dichloromethane/light petroleum (1:1) afforded a major red band of (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)-copper(II) (**8a**) (53 atom % deuterium, 61 mg, 67%), MS m/z 680 (10%), 679 (25), 678 (57), 677 (75), 676 ([^{2}H]M^+, 100), 675 ([^{1}H]-M^+, 63). This product cochromatographed with and had the same electronic spectrum as the corresponding unlabeled (5,10,15,20-tetraphenylporphyrinato)copper(II).[30]

(2,3-Dihydro-5,10,15,20-tetraphenyl-[2-$^2H_1$]porphyrinato)-copper(II) (7). A solution of (2,3-dihydro-2-nitro-5,10,15,20-tetraphenyl[3-$^2H_1$]porphyrinato)copper(II) (**6a**) (79 mg, 0.11 mmol), AIBN (40 mg, 0.24 mmol), and tributyltin hydride (1.5 mL) in dry benzene (50 mL) was heated at reflux under nitrogen for 2 h. On cooling, the solvent was removed by rotary evaporation. The residue was triturated with light petroleum (2 × 50 mL) and filtered. The residue was triturated with dichloromethane/light petroleum (1:1, 2 × 50 mL) and filtered. The filtrate was chromatographed on a silica column (4 cm diameter, 250 g) eluted with dichloromethane/light petroleum (1:1) and the front running, major, blue-green band was collected, evaporated to dryness, and combined with the undissolved residue to yield (2,3-dihydro-5,10,15,20-tetraphenyl[2-$^2H_1$]porphyrinato)-copper(II) (**7**) (56 mg, 76%): mp >350 °C; IR ν_{max} (Nujol) 1560, 1045, 990 cm^{-1}; UV and vis λ_{max} ($CHCl_3$) 395sh, 416, 510, 542, 595, 618 nm (log ϵ 4.63, 5.38, 3.61, 3.84, 3.98, 4.30); MS m/z 681 (19%), 680 (44), 679 (58), 678 (M^+, 100), 677 (77), 676 (M − 2H, 96), 675 (M − ^{2}H, 58). The visible spectrum of this product was consistent with the visible spectra data of the corresponding unlabeled material and the two compounds cochromatographed.[22]

(5,10,15,20-Tetraphenyl[2-^{2}H]porphyrinato)zinc(II) (8b). Method A: Introduction of Deuterium Label at the β-Pyrrolic Position Adjacent to That Originally Occupied by the Nitro Group. A solution of (2-nitro-5,10,15,20-tetraphenylporphyrinato)zinc(II)[20,21] (**5b**) (83 mg, 0.11 mmol) in dry, distilled Me_2SO (40 mL) was stirred with sodium borodeuteride (98 atom % deuterium, 40 mg, 0.95 mmol) for 4 h. The mixture was then diluted with dichloromethane (100 mL), washed with water (6 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The crude nitrochlorin was chromatographed on a silica column (4 cm diameter, 200 g) eluted with dichloromethane/light petroleum (1:1) to yield (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)zinc(II) (**8b**) (51 atom % deuterium, 35 mg, 47%): ^1H NMR δ ($CDCl_3$) 7.72–7.81 (12 H, m, *m* and *p*-Ph), 8.20–8.25 (8 H, m, *o*-Ph), 8.95 (7.5 H, s, β-pyrrolic H); MS m/z 682 (21%), 681 (38), 680 (48), 679 (66), 678 (67), 677 ([^{2}H]M^+, 100), 676 ([^{1}H]M^+, 64), 675 (30). This compound cochromatographed with and had a UV and vis spectrum essentially identical to that of an authentic sample of corresponding unlabeled compound.[30,31]

Method B: Introduction of Deuterium Label at the β-Pyrrolic Position Previously Occupied by the Nitro Group. To a solution of (2-nitro-5,10,15,20-tetraphenylporphyrinato)zinc(II)[20,21] (**5b**) (100 mg, 0.14 mmol) in dry, distilled Me_2SO (25 mL) was added D_2O (100.0 atom % D, 0.25 mL) followed by sodium borohydride (100 mg, 2.4 mmol) and the mixture was stirred for 1 h. The mixture was then diluted with further D_2O (100.0 atom % deuterium, 2.25 mL) and the blue-green mixture was well stirred for 30 min. Dichloromethane (80 mL) was added and the organic layer was washed with water (6 × 50 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The crude nitrochlorin **9** was taken up in chloroform (20 mL) and adsorbed onto silica (Merck silica gel 60 HR, type 7744, 10 g), stirred at 50 °C for 30 min, during which time the color became purple-red, and then the solvent was removed on a rotary evaporator at 50 °C. The silica was added to the top of a short column (8 cm diameter × 8 cm length) of the same silica type and the whole was eluted with dichloromethane/light petroleum (1:1). Workup of the first (crimson-pink) band yielded (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)zinc(II) (**8b**) as a crimson solid (>98 atom % deuterium, 39 mg, 42%), mp >350 °C; ^1H NMR δ ($CDCl_3$) 7.72–7.81 (12 H, m, *m* and *p*-Ph), 8.20–8.25 (8 H, m, *o*-Ph), 8.95 (7.0 H, s, β-pyrrolic H); MS m/z 683 (12%), 682 (35), 681 (60), 680 (55), 679 (76), 678 (70), 677 (M^+, 100). This

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(31) Barnett, G. H.; Hudson, M. F.; McCombie, S. W.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 691–696.

compound also cochromatographed with the corresponding unlabelled (5,10,15,20-tetraphenylporphyrinato)zinc(II).[30,31]

(2-Nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (5c). To a stirred solution/suspension of (5,10,15,20-tetraphenylporphyrinato)nickel(II)[32] (500 mg, 0.75 mmol) in chloroform (1 L) was added a solution of nitrogen dioxide in light petroleum (0.5% (w/v), 15 mL) over a period of 6 h. The mixture was then evaporated to dryness. The residue was chromatographed over a silica column (10 cm diameter, 600 g) eluted with chloroform/light petroleum (1:1) to yield a red, front-running band of unreacted (5,10,15,20-tetraphenylporphyrinato)nickel(II) (43 mg, 9%) and a major, red-green band of (2-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**5c**) (391 mg, 73%), which was recrystallized from chloroform/hexane as purple microcrystals: mp >350 °C; IR ν_{max} (Nujol) 1525 (NO_2), 1345 cm^{-1} (NO_2); UV λ_{max} ($CHCl_3$) 383, 431, 541, 585 nm (log ϵ 4.51, 5.16, 4.08, 3.98); ^1H NMR δ ($CDCl_3$) 7.56–7.77 (12 H, m, *m*- and *p*-Ph), 7.93–8.02 (8 H, m, *o*-Ph), 8.63 and 8.66 (2 H, ABq, J_{AB} 5 Hz, β-pyrrolic H), 8.64 and 8.72 (2 H, ABq, J_{AB} 5 Hz, β-pyrrolic H), 8.67 and 8.71 (2 H, ABq, J_{AB} 5 Hz, β-pyrrolic H), 8.99 (1 H, s, C(3)H); MS *m/z* 718 (10%), 717 (18), 716 (16), 715 (M^+, 31), 689 (19), 688 (32), 687 (50), 686 (55), 685 (M – NO, 100), 684 (18), 683 (28). Anal. Calcd for $C_{44}H_{27}N_5NiO_2$: C, 73.8; H, 3.8; N, 9.8. Found: C, 73.9; H, 3.6; N, 9.7.

(5,10,15,20-Tetraphenyl[2-^{2}H]porphyrinato)nickel(II) (8c). A slurry of (2-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**5c**) (110 mg, 0.154 mmol) in dry, distilled Me_2SO (50 mL) was stirred with sodium borodeuteride (98 atom % deuterium, 55 mg, 1.31 mmol) under nitrogen for 5 h. The mixture was diluted with dichloromethane (200 mL), washed with water (6 × 200 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The crude nitrochlorin was chromatographed on a silica column (4 cm diameter, 300 g) eluted with dichloromethane/light petroleum (7:3) to yield a front running red band of (5,10,15,20-tetraphenyl[2-^{2}H]porphyrinato)nickel(II) (**8c**) (55 atom % deuterium, 20 mg, 20%), ^1H NMR δ ($CDCl_3$) 7.64–7.73 (12 H, m, *m*- and *p*-Ph), 7.99–8.04 (8 H, m, *o*-Ph), 8.75 (7.5 H, s, β-pyrrolic H); *m/z* 675 (10%), 674 (30), 673 (60), 672 (72), 671 ([^{2}H]M^+, 100), 670 ([^{1}H]M^+, 58). The compound cochromatographed with and had UV and vis essentially identical with that of the corresponding unlabeled compound, (5,10,15,20-tetraphenylporphyrinato)nickel(II).[30,32] A more polar red-green band afforded starting nitroporphyrin **5c** (82 mg, 75%), identical in all respects to authentic material.

(2-Methoxy-3-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (10). To a solution of (2-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**5c**) (99 mg, 0.14 mmol) in DMF (20 mL) was added solid sodium methoxide (31 mg, 0.57 mmol), and the mixture was stirred under nitrogen for 16 h. The mixture was then diluted with dichloromethane (100 mL), washed with water (6 × 200 mL), dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was chromatographed over silica. The second, red band gave (2-methoxy-3-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) **10** (16 mg, 16%) which recrystallized from dichloromethane/hexane as fine red microcrystals: mp 301–303 °C; IR ν_{max} (Nujol) 1570 cm^{-1} (NO_2); UV and vis λ_{max} ($CHCl_3$) 380sh, 425, 540, 578sh nm (log ϵ 4.30, 5.17, 4.15, 3.81); ^1H NMR δ ($CDCl_3$) 3.74 (3 H, s, OCH_3), 7.54–7.74 (12 H, m, *m*- and *p*-Ph), 7.83–7.88 (2 H, m, H_o at 20-Ph), 7.90–8.01 (6 H, m, H_o at 5-, 10- and 15-Ph), 8.54 and 8.66 (2 H, ABq, J_{AB} = 5 H, β-H), 8.62 (2 H, s, 12- and 13-H), 8.65 and 8.71 (2 H, ABq, J_{AB} = 5 Hz, β-H)); MS *m/z* 749 (13), 748 (26), 747 (54), 746 (55), 745 (M^+, 100), 717 (17), 716 (18), 715 (29), 703 (13), 702 (26), 701 (28), 700 (44), 699 (17), 698 (13), 697 (12), 688 (13), 687 (13), 686 (20), 685 (18), 684 (13), 683 (13), 668 (16). Anal. Calcd for $C_{45}H_{29}N_5NiO_3$: C, 72.4; H, 3.9; N, 9.4. Found: C, 72.6; H, 3.9; N, 9.4.

(5,10,15,20-Tetraphenyl[2-^{2}H]porphyrinato)nickel(II) (8c) and (2-nitro-5,10,15,20-tetraphenyl[3-^{2}H]porphyrinato)nickel(II) (12). A suspension of (2-methoxy-3-nitro-5,10,15,20-tetraphenylporphyrinato)nickel(II) (**10**) (40 mg, 0.054 mmol) in dry, distilled Me_2SO (40 mL) was stirred with sodium borodeuteride (98% deuterium content, 20 mg, 0.48 mmol) for 15 min. The mixture was then diluted with dichloromethane (50 mL), washed with water (6 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The residue was chromatographed on a silica column (4 cm diameter, 200 g) eluted with dichloromethane/light petroleum (1:1). The front running, blue band gradually turned red on the column and was collected and evaporated to dryness to yield (5,10,15,20-tetraphenyl[2-^{2}H]-porphyrinato)nickel(II) (**8c**) (<98 atom % deuterium, 13 mg, 36%): mp >350 °C; IR ν_{max} (Nujol) 1590, 1170, 1065, 995 cm^{-1}; UV and vis λ_{max} ($CHCl_3$) 416, 490s, 529, 614 nm (log ϵ 5.34, 3.51, 4.19, 2.69); ^1H NMR δ ($CDCl_3$) 7.64–7.73 (12 H, m, *m*- and *p*-Ph), 7.99-8.04 (8 H, m, *o*-Ph), 8.75 (7.0 H, s, β-pyrrolic H); MS *m/z* 675 (17%), 674 (28), 673 (58), 672 (60), 671 (M^+, 100).

The more polar, reddish-green band was collected to yield on evaporation (2-nitro-5,10,15,20-tetraphenyl[3-^{2}H]porphyrinato)-nickel(II) (**12**) (>98 atom % deuterium, 21 mg, 54%), mp >350 °C; ^1H NMR δ ($CDCl_3$) 7.56–7.77 (12 H, m, *m*- and *p*-Ph), 7.93–8.02 (8 H, m, *o*-Ph), 8.64 and 8.71 (2 H, ABq, *J* 5 Hz, β-pyrrolic H), 8.65 (2 H, ABq, spacing 5 Hz, β-pyrrolic H), 8.67 and 8.72 (2 H, ABq, *J* 5 Hz, β-pyrrolic H); MS *m/z* 720 (17%), 719 (30), 718 (55), 717 (58), 716 (M^+, 100), 715 (18), 689 (20), 688 (36), 687 (58), 686 (72), 685 (79), 684 (36), 683 (48), 672 (14), 671 (18), 670 (24), 669 (18), 668 (11), 667 (12).

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Convenient Novel Syntheses of 1,1-Bis(heteroaryl)alkanes

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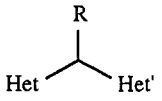
A variety of symmetrical 1,1-bis(heteroaryl)alkanes are prepared in excellent yields from the reaction of *N*-(α-benzotriazolylalkyl)carbamate **2** (itself easily available from the condensation of benzotriazole, an aldehyde, and an alkyl carbamate) with an excess of 2-methylthiophene or 2-methylfuran. When methyl *N*-(α-benzotriazolylalkyl)carbamate **2a** is treated with 1 equiv of a heterocycle, the benzotriazolylalkyl-substituted heterocycle is formed. These intermediates react further with other heterocycles to give unsymmetrical 1,1-bis(heteroaryl)alkanes in good yields under mild conditions.

Bis(heterocyclyl)methanes are of interest to the food industry as they are present as natural compounds in food and beverage items such as licorice;[1] for example, difuryl- and dithienylalkanes are flavor agents in coffee.[2,3] Many bis(heterocyclyl)methanes are also of importance in dyestuff chemistry as they are readily oxidized to the corresponding cyanine dyes.[4] Furthermore, 1,1-bis(heterocyclyl)alkanes are important intermediates in the synthesis of various heterocyclic macromolecules;[5] for example, dipyrromethanes have been widely used as synthetic intermediates in total syntheses of porphyrins.[6] The action of dichloromethyl alkyl ether and tin(IV) chloride on (diheteroaryl)methanes is a useful route to polycyclic heteroaromatic systems.[7]

Several synthetic routes to bis(heteroaryl)methanes **1** are known, but none is both general and convenient.



1

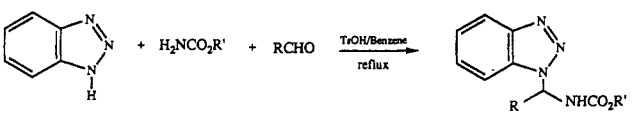
Many are only applicable to the preparation of symmetrical bis(heterocyclyl)methanes. Di-2-furylmethane has been prepared by the reduction of di-2-furyl ketone[8] and also by the interaction of 2-chloromercurifuran and furfuryl chloride.[9] Reduction of the corresponding (diheteroaryl)-methanols also gives (diheteroaryl)methanes.[7] However, most of these methods are limited to the preparation of compounds in which an unsubstituted methylene group links the two heteroaromatic rings (**1**, Het = Het′, R = H), and their utility is further restricted by the inaccessibility of suitable diheteroaryl ketones and methanols. The reaction of a (heteroaryl)lithium with a (heteroaryl)methyl chloride[7] gives a (diheteroaryl)methane, but it requires severe conditions. Thiophenes, furans, and pyrroles with free α-positions are susceptible to electrophilic attack by aldehydes or ketones, and this is a well-known route to (diheteroaryl)methane derivatives.[10] However, this type of condensation generally requires a strong inorganic acid catalyst, such as 75% H_2SO_4[11] or hydrochloric acid.[12] These experimental conditions present the drawback of causing resinification[13] and degradation[14] of the heterocyclic rings of substrates and products. An improvement of this condensation using macroporous ion-exchange resins as catalyst[15] is satisfactory for the preparation of difuryl and dithienyl derivatives.

Unsymmetrical bis(heterocyclyl)methanes are far less explored; in fact, some structurally simple bis(heterocyclyl)methanes, especially with two different heterocyclic ring systems, are not known. The few synthetic procedures available have only led to a limited number of compounds of this class. Perhaps the most important is the reduction of the corresponding alcohols. Sodium borohydride–trifluoroacetic acid reduction of (diheteroaryl)methanols gives (diheteroaryl)methanes in 32–76% yield;[16] however, use of this reduction method has been confined to the methylene derivatives (**1**, R = H). Moreover, the prep-

Table I. Preparation of *N*-(1-Benzotriazolylalkyl)carbamates

compd	R	R′	mp (°C)	yield (%)	molecular formula	found (required) C	H	N
2a	iPr	Me	118–120	84	$C_{12}H_{16}N_4O_2$	58.05 (58.05)	6.53 (6.50)	22.44 (22.57)
2b	Ph	Me	123–124	78	$C_{15}H_{14}N_4O_2$	63.87 (63.82)	5.03 (5.00)	19.90 (19.85)
2c	H	Me	155–156	74	$C_9H_{10}N_4O_2$	52.38 (52.42)	4.86 (4.89)	27.45 (27.17)
2d	Ph	Ph	162–164	69	$C_{20}H_{16}N_4O_2$	69.59 (69.76)	4.73 (4.68)	16.27 (16.27)

Scheme I



2

2a: R = i-Pr, R'=Me 84%
2b: R = Ph, R'=Me 78%
2c: R=H, R'=Me 74%
2d: R=R'=Ph 69%

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Table II. ^{1}H NMR Data of *N*-(1-Benzotriazolylalkyl)carbamates

	benzotriazole (each H)						
compd	H4	H5	H6	H7	NH (1H)	OMe (3H, s)	other signals
2a	8.10 (d, J = 9.0 Hz)	7.43 (t, J = 7.5 Hz)	7.59 (t, J = 7.6 Hz)	8.08 (d, J = 8.4 Hz)	8.91 (d, J = 8.7 Hz)	5.36	6.15 (t, J = 9.0 Hz, 1H, CH), 2.71 (m, 1H, CHMe$_2$), 1.18 (d, J = 6.6 Hz, 3H, CH_3), 0.57 (d, J = 6.6 Hz, 3H, CH_3)
2b	8.12 (d, J = 8.3 Hz)	7.41 (m, overlapped by PhH)	7.56 (t, J = 7.9 Hz)	7.95 (d, J = 8.4 Hz)	9.47 (d, J = 8.5 Hz)	3.64	7.86 (d, J = 8.6 Hz, 1H, CH), 7.41 (m, 5H, Ph-H)
2c	8.03 (d, J = 8.3 Hz)	7.39 (t, J = 7.6 Hz)	7.52 (t, J = 6.9 Hz)	7.94 (d, J = 8.3 Hz)	6.55 (s)	3.71	6.06 (d, J = 6.8 Hz, 2H, CH_2)
2d	8.12 (d, J = 8.3 Hz)	7.44 (m, overlapped by PhH)	7.44 (m, overlapped by PhH)	7.86 (m, overlapped by PhH)	10.0 (d, J = 8.5 Hz)		7.86 (m, 2H, Ph-H), 7.44 (m, 7H, Ph-H), 7.18 (m, 1H, CH), 7.18 (m, 1H, Ph-H)

Table III. ^{13}C NMR Data of *N*-(1-Benzotriazolylalkyl)carbamates

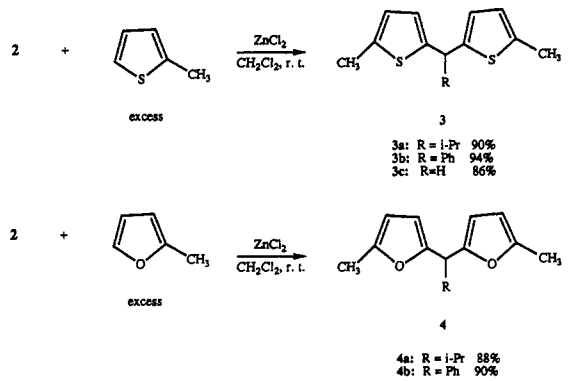
	benzotriazole							
compd	C_4	C_5	C_6	C_7	C_{3a}	C_{7a}	CO	other carbons
2a	119.2	127.2	124.0	111.1	145.2	132.0	156.3	71.9 (CH), 51.7 (OCH_3), 31.4 (CH), 19.1 (CH_3), 18.2 (CH_3)
2b	119.2	127.4	124.1	111.1	145.3	131.5	156.1	135.9 (Ph), 128.7 (Ph), 128.5 (Ph), 126.5 (Ph), 68.2 (CH), 52.1 (OCH_3)
2c	119.4	127.9	124.4	110.8	146.0	132.4	156.8	53.5 (CH_2), 52.8 (OCH_3)
2d	119.4	127.7	124.3	111.2	145.5	131.7	154.2	150.5 (Ph), 135.7 (Ph), 129.4 (Ph), 129.0 (Ph), 128.7 (Ph), 126.9 (Ph), 125.5 (Ph), 121.7 (Ph), 68.1 (CH)

Table IV. Preparation of Symmetrical 1,1-Bis(heteroaryl)alkanes

						HRMS/analysis			
						found		required	
compd	heteroaryl	R	mp (°C)	yield (%)	molecular form	C	H	C	H
3a	5-methylthiophen-2-yl	iPr	45–46	90	$C_{14}H_{18}S_2$	67.07	7.26	67.15	7.25
3b	5-methylthiophen-2-yl	Ph	oil	94	$C_{17}H_{16}S_2$	284.0717		284.0694	
3c	5-methylthiophen-2-yl	H	oil	86	$C_{11}H_{12}S_2$	208.0370		208.0380	
4a	5-methylfur-2-yl	iPr	oil	88	$C_{14}H_{18}O_2$	218.1304		218.1307	
4b	5-methylfur-2-yl	Ph	oil	90 (65)[a]	$C_{17}H_{16}O_2$	252.1167		252.1150	

[a] From phenyl *N*-(1-benzotriazol-1-yl)carbamate (**2d**).

Scheme II



aration of (diheteroaryl)methanols usually requires lithiation under severe conditions. Alkyl α-methoxy- and α-hydroxypyrrylacetates interact with *N*-methylindole in the presence of Lewis acids to give diarylacetic esters,[17] but the starting materials are not easily available and this method is not general. Condensation of an α-(acetoxymethyl)pyrrole with an appropriately substituted pyrrole with a free α-position in acetic acid,[18] in the presence of toluene *p*-sulfonic acid[19] or Montmorillonite clay,[20] produces unsymmetrical dipyrrolylmethanes. However, the isolation of the product from tarry reaction byproducts is tedious.[20] Symmetrical pyrrolylmethanes are often formed as byproducts by self-condensation of the (acetoxymethyl)-pyrrole,[21,22] and the method is useful only for the fully substituted dipyrrolylmethanes in order to avoid polymerization. Unsymmetrical difurylmethanes are obtained from the reaction of [(5-methylfuryl)phosphinyl]carbinol and furan followed by a Wittig–Horner reaction,[23] but this method is not general. Alkylation of furan, thiophene, and pyrrole with furfuryl alcohol in the presence of the strongly acidic Amberlyst 15 cation-exchange resin affords the respective (2-furylheteroaryl)methanes;[24] however, the yields are low and purification is difficult (preparative GLC) because of the formation of difurylmethyl ether and resinous byproducts.

We now report a general and convenient method for the preparation of both symmetrical and unsymmetrical bis-heterocyclic alkanes using benzotriazole as a synthetic auxiliary. Recent work in our laboratory has shown the utility of the benzotriazole anion as a leaving group, with

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