at δ 6.29, a two-proton multiplet at δ 3.45–3.33, a one-proton multiplet centered at δ 3.22, a one-proton multiplet centered at δ 3.08, a one-proton doublet of doublets, part of an ABX system (J = 3.13, 11.52 Hz), centered at δ 82.79, and a two-proton bridge AB quartet (J_{AB} = 8.49 Hz) at δ_A 1.61 and δ_B 1.45. The infrared spectrum ($CHCl_3$) showed absorbance at 2960 (m), 2945 (m), 2870 (w), 1695 (s, shoulder), 1674 (vs), 1445 (w), 1342 (m), 1130 (m), 1100 (m), 1070 (m), 962 (w), and 915 cm^{-1} (w). The mass spectrum (70 eV) showed peaks at m/e (relative intensity) 166 (100, M^+), 138 (17, $M^+ - CO$), 124 (21), 105 (17, $M^+ - CHSO$), 101 (21, $M^+ - C_5H_5$), 92 (17, $M^+ - C_2H_2SO$), 91 (21, $M^+ - 2H_3SO$), and 66 (67, $M^+ - C_4H_4SO$). Exact mass calcd for $C_9H_{10}SO$ 166.04524, found 166.0458.

2-(Trimethylsiloxy)thiophene (XV). A solution of 0.606 g (6.6 mmol) of 3-thiolen-2-one (I) and 0.918 g (9.09 mmol) of anhydrous trimethylamine in 10 mL of anhydrous ether was treated under an inert atmosphere with 0.826 g (7.575 mmol) of chlorotrimethylsilane. The resulting white suspension was stirred 5 h at room temperature. The reaction mixture was diluted with 30 mL of pentane and filtered by suction through a pad of Celite 545. The filtrate was concentrated on a rotary evaporator and then distilled bulb-to-bulb at 23 °C (0.03 mm) into a liquid nitrogen cooled trap. The product, 0.694 g (66%) of a colorless oil, was shown to be pure by NMR analysis.

The 300-MHz spectrum ($CDCl_3$) of XV showed a one-proton doublet of doublets (J = 3.64, 5.86 Hz) at δ 6.61, a one-proton doublet of doublets (J = 1.42, 5.86 Hz) at δ 6.51, a one-proton doublet of doublets (J = 1.42, 3.64 Hz) at δ 6.15, and nine-proton trimethylsilyl ether singlet at δ 0.29. The infrared spectrum ($CHCl_3$) showed bands at 2960 (w), 1540 (w), 1460 (m), 1260 (m), 1190 (s), 880 (s), 849 cm^{-1} (s). Hydrolysis of XV to the starting thiolenone is very ready and accounts for the small carbonyl doublet at 1690 and 1710 cm^{-1} observed in the infrared spectrum. The mass spectrum (70 eV) showed peaks at m/e (relative intensity) 172 (100, M^+) 100 (11, $M^+ + H - C_3H_9Si$), and 73 (11, C_3H_9Si). exact mass calcd for $C_7H_{12}OSSi$ 172.0378, found 172.0371.

Reaction of 3-Thiolen-2-one (I) with (1*E*)-1-Methoxy-3-(trimethylsiloxy)-1,3-butadiene. In an NMR tube were placed 0.047 g (0.47 mmol) of 3-thiolen-2-one (I), 0.081 g (0.47 mmol) of (1*E*)-1-methoxy-3-(trimethylsiloxy)-1,3-butadiene (XIV), and 0.50 mL of chloroform-*d*. The tube was heated at 55 °C for 50 h. At this time, the 300-MHz NMR spectrum revealed little remaining diene. In addition to small signals due to 3-thiolen-2-one, the spectrum showed 2-(trimethylsiloxy)thiophene and 4-methoxybut-3-en-2-one. Minor product peaks in the atomatic and vinyl region were observed but were not investigated further.

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Registry No. I, 3354-32-3; III, 513-81-5; IV, 83043-39-4; V, 592-57-4; VI, 83043-40-7; VII, 2082-08-8; VIII, 83043-41-8; (*E*,*E*)-IX, 15910-11-9; X, 83043-42-9; XI, 1194-57-6; XII, 542-92-7; XIII, 83043-43-0; (*E*)-XIV, 54125-02-9; XV, 83043-44-1; 4-methoxybut-3-en-2-one, 4652-27-1.

Synthesis of 3,4-Bis(trifluoromethyl)pyrroles

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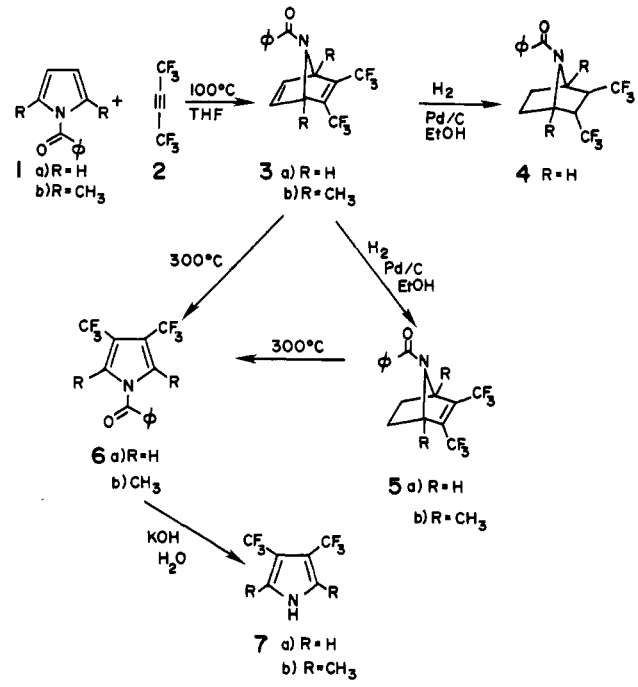
Current research directed toward the synthesis of octakis(polyfluoroalkyl)porphyrins required the preparation of 3,4-bis(trifluoromethyl)pyrroles **7a** and **7b**. The general procedure for the synthesis of these substituted pyrroles which we describe here (Scheme I) gives much higher overall yields than a method recently reported for the preparation of **7a**.[1] Heating *N*-benzoylpyrrole (**1a**) with hexafluoro-2-butyne affords a quantitative yield of the adduct **3**.[2,3] Pyrolysis of **5**, prepared by the hydrogenation of **3**, cleanly cleaves ethylene, yielding **6**. The more direct route, pyrolysis of **3**, gave mainly unreacted starting material **3**, the retro-Diels–Alder product **1**, and only a trace of **6**. Basic hydrolysis of **6** gave **7**. The overall yield for this route (**1** → **3** → **5** → **6** → **7**) is 83%.

Scheme I



Experimental Section

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were measured on a Perkin-Elmer 237 grating spectrophotometer. Mass spectra were obtained on a Finnigan 4000 instrument at 70 eV. NMR spectra (in $CDCl_3$, Me_4Si as an internal standard) were recorded on a Varian T-60 at 60 MHz for ^1H spectra and on a Bruker WM-250 at 62.9 MHz for ^{13}C spectra. Elemental analyses were performed by Galbraith Laboratories Inc. *N*-Benzoylpyrrole and *N*-benzoyl-2,5-dimethylpyrrole were prepared as previously described.[4] Hexafluorobut-2-yne was purchased (Columbia) and used without prior purification.

***N*-Benzoyl-2,3-bis(trifluoromethyl)-7-azabicyclo[2.2.1]-2,5-heptadiene (3a).** Hexafluorobut-2-yne (**2**; 7.60 g, 46.9 mmol) was condensed at −78 °C into a heavy-walled glass tube containing *N*-benzoylpyrrole (**1a**; 4.0 g, 23.4 mmol) and THF (15 mL). The sealed tube was heated inside a steam bath for 5 h. The solvent and excess **2** were evaporated on a rotary evaporator, affording 7.79 g (100%) of **3a** as a yellow oil. This product appeared pure by NMR and TLC and was used directly in the preparation of **4** and **5a**: ^1H NMR δ 5.56 (2 H, br s, H-1 and H-4), 7.10 (2 H, m, H-5 and H-6), 7.35 (5 H, br s, aromatic); ^{13}C NMR δ 66.59, 69.76, (C-1 and C-4), 120.89 (q, J = 269.8 Hz, CF_3), 128.10, 128.86, 132.16, 132.80 (aromatic carbons), 144.48, 142.65 (C-5 and C-6), 148.98 (br, C-2 and C-3), 169.12 (C=O); mass spectrum, m/e (relative intensity) 333 (M^+, 10), 105 (100), 77 (40), 51 (13); IR (neat) 3250, 3060, 1675, 1350, 1290, 1180, 1130 cm^{-1}.

***N*-Benzoyl-2,3-bis(trifluoromethyl)-1,4-dimethyl-7-azabicyclo[2.2.1]-2,5-heptadiene (3b).** Pyrrole **3b** was prepared

(1) Leroy, J.; Cantacuzene, D.; Wakselman, C. *Synthesis* **1982**, 313.
(2) Pyrrole and *N*-methylpyrrole give complex mixtures of adducts with **2**. Blazejewski, C. J.; Cantacuzene, D.; Wakselman, C. *Tetrahedron Lett.* **1975**, 363.
(3) 3,4-Bis(trifluoromethyl)furan has been prepared by this method. Weis, C. D. *J. Org. Chem.* **1962**, *27*, 3520.
(4) Jones, R. A.; Lasalett, R. L. *Aust. J. Chem.* **1964**, *17* 1056.

0022-3263/82/1947-4779$01.25/0

as above in 100% yield by heating **2** and **1b** for 9 h: ^{1}H NMR δ 1.67 (6 H, s, CH_3), 6.80 (2 H, s, CH), 7.40 (5 H, m, aromatic); ^{13}C NMR δ 16.00 (CH_3), 78.44 (C-1 and C-4), 121.76, (q, J = 273.0 Hz, CF_3), 128.49, 129.24, 132.39, 137.28, (aromatic carbons), 148 (C-5 and C-6), 150.90, (m, C-2 and C-3), 174.7 (C=O); mass spectrum (CI, CH_4), m/e 362 ($M^+ + 1$); IR (neat) 3300, 3000, 1660, 1450, 1325, 1250, 1150, 700 cm^{-1}.

***N*-Benzoyl-2,3-bis(trifluoromethyl)-7-azabicyclo[2.2.1]heptane (4).** A solution of **3a** (0.50 g, 1.5 mmol) in EtOH (20 mL) was hydrogenated in a Parr apparatus at 75 lbs/in.^{2} of H_2 for 2 h in the presence of 10% palladium on activated carbon (10 mg). The solution was filtered and concentrated in vacuo. The resulting solid was crystallized from hexane, yielding 0.49 g (97%) of **4** as colorless crystals: mp 114–115 °C; ^{1}H NMR δ 2.00 (4 H, m, CH_2), 3.06 (2 H, m, CH), 4.60 (2 H, m, CH), 7.40 (5 H, m, aromatic); ^{13}C NMR δ 24.05 (C-5 and C-6), 44.88 (C-2 and C-3), 58.86 (C-1 and C-4), 124.65 (q, J = 280.5 Hz, CF_3), 128.13, 128.84, 131.92 134.08 (aromatic carbons), 169.98 (C=O); mass spectrum, m/e (relative intensity) 337 (M^+, 21), 105 (100), 77 (33), 51 (8); IR (Nujol) 3300, 1630, 1410, 1305, 1275, 1230, 725 cm^{-1}.

Anal. Calcd for $C_{15}H_{13}NOF_6$: C, 53.41; H, 3.86. Found C, 53.42; H, 3.99.

***N*-Benzoyl-2,3-bis(trifluoromethyl)-7-azabicyclo[2.2.1]-2-heptene (5a).** A solution of **3a** (2.65 g, 7.96 mmol) in EtOH (20 mL) was hydrogenated at 1 atm of H_2 in the presence of 10% palladium on activated carbon (30 mg). The uptake of hydrogen dropped sharply after 1 equiv (180 mL), and the solution was filtered and concentrated in vacuo, yielding 2.58 g (97%) of **5a** as a yellow oil. The product appeared pure by NMR and TLC and was used directly in the preparation of **6a**: ^{1}H NMR δ 1.47 (2 H, m, CH_2), 2.13 (2 H, m, CH_2), 5.13 (2 H, m, CH), 7.36 (5 H, br s, aromatic); ^{13}C NMR δ 24.15 (C-5 and C-6), 61.41 (C-1 and C-4), 120.2 (q, J = 271.3 Hz, CF_3), 128.86, 128.88, 131.95, 133.30 (aromatic carbons), 139.44 (C-2 and C-3), 169.47 (C=O); mass spectrum (CI, CH_4), m/e 336 ($M^+ + 1$); IR (neat) 3250, 3050, 2960, 1670, 1370, 1300, 1180, 1150, 1040, 730, 710 cm^{-1}.

***N*-Benzoyl-2,3-bis(trifluoromethyl)-1,4-dimethyl-7-azabicyclo[2.2.1]-2-heptene (5b).** Hydrogenation of **3b** as above gave **5b** (95% yield) as a yellow oil: ^{1}H NMR δ 1.53 (6 H, s, CH_3), 1.58 (2 H, m, CH_2), 2.03 (2 H, m, CH_2), 7.40 (5 H, m, aromatic); ^{13}C NMR 18.41 (CH_3), 34.39 (C-5 and C-6), 72.79 (C-1 and C-4), 121.24 (q, J = 273.7 Hz, CF_3), 128.43, 129.52, 132.47, 138.00 (aromatic carbons), 140.90 (m, C-2 and C-3), 176.43 (C=O); mass spectrum (CI, CH_4), m/e 364 ($M^+ + 1$); IR (neat) 3260, 2950, 1675, 1450, 1335, 1270, 1170, 945, 840, 760, 710 cm^{-1}.

***N*-Benozyl-3,4-bis(trifluoromethyl)pyrrole (6a).** A solution of **5a** (2.20 g, 6.57 mmol) in benzene (100 mL) was passed dropwise in a slow stream of nitrogen through a tube packed with glass beads and heated to 300 °C. The product was collected in a flask cooled to −78 °C. The column was washed with additional benzene (20 mL), and the solution was concentrated in vacuo. Distillation (0.15 mm, 84 °C) gave 1.90 g (94%) of **6a** as a colorless oil: ^{1}H NMR δ 7.56 (7 H, m, aromatic and α-pyrrole); ^{13}C NMR δ 115.70 (q, J = 37.7 Hz, β-pyrrole carbons), 121.75, (q, J = 270.5 Hz, CF_3), 123.5 (α-pyrrole carbons), 129.40, 130.00, 130.70, 134.20 (aromatic carbons), 166.50 (C=O); mass spectrum (CI, CH_4), m/e 308 ($M^+ + 1$); IR (neat) 3360, 3160, 1730, 1560, 1320, 1250, 1150, 980, 900, 725 cm^{-1}.

***N*-Benzoyl-3,4-bis(trifluoromethyl)-2,5-dimethylpyrrole (6b).** Pyrolysis of **5b** as above gave **6b** (95% yield) as colorless crystals from hexane: mp 69.5–70.5 °C; ^{1}H NMR δ 2.17 (6 H, s, CH_3), 7.60 (5 H, m, aromatic); ^{13}C NMR δ 12.00 (CH_3), 110.09 (q, J = 38.8 Hz, β-pyrrole carbons), 116.92 (α-pyrrole carbons), 123.35, (q, J = 269.1 Hz, CF_3), 129.78, 130.81, 133.16, 135.85 (aromatic carbons), 169.98 (C=O); mass spectrum, m/e (relative intensity) 335 ($M^+ + 1$), 105 (100) 77 (57), 51 (11); IR (Nujol) 3350, 1725, 1370, 1260, 1200, 1150, 1110, 925, 725 cm^{-1}.

Anal. Calcd for $C_{15}H_{11}NOF_6$: C, 53.73; H, 3.28. Found C, 53.73; H, 3.31.

3,4-Bis(trifluoromethyl)pyrrole (7a). A solution of **6a** (1.30 g, 4.23 mmol) and KOH (0.24 g, 1 equiv) in diethyl ether (60 mL) and water (3 mL) was stirred at room temperature for 6 h. The reaction was monitored by TLC (silica, CH_2Cl_2), and additional KOH was added in small amounts as needed. Water (200 mL) was added, and the solution was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Recrystallization from hexane–$CHCl_3$ (3:1) gave 0.77 g (90%) of **7a** as volatile, colorless crystals: mp 36.5–37.5 °C; ^{1}H NMR δ 7.16 (2 H, d, J = 3 Hz), 8.53 (1 H, br s, NH); ^{13}C NMR δ 112.75 (q, J = 39.0 Hz, β-pyrrole carbons), 121.18 (α-pyrrole carbons), 122.96 (q, J = 266.7 Hz, CF_3); mass spectrum, m/e (relative intensity) 203 (M^+, 38), 184 (100), 153 (8), 134 (3); IR (neat) 3475, 3300, 1560, 1450, 1370, 1330, 1230, 1130, 980.

Anal. Calcd for $C_6H_3NF_6$: C, 35.47; H, 1.48. Found: C, 35.00; H, 1.51.

3,4-Bis(trifluoromethyl)-2,5-dimethylpyrrole (7b). A solution of **6b** (2.00 g, 5.97 mmol) and KOH (0.34 g, 1 equiv) in THF (130 mL) and water (7 mL) was stirred at room temperature for 6 h. The reaction was monitored by TLC (silica, hexane–CH_2Cl_2), and additional KOH was added in small amounts as needed. Water (300 mL) was added, and the solution was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Recrystallization from hexane gave 1.27 g (92%) of **7b** as colorless crystals: mp 95.5–96.5 °C; ^{1}H NMR δ 2.27 (6 H, s, CH_3). 7.87 (1 H, br, s, NH); ^{13}C NMR δ 12.04 (CH_3), 108.23 (q, J = 39.7 Hz, β-pyrrole carbon), 123.89 (q, J = 267.3 Hz, CF_3), 128.94 (α-pyrrole carbon); mass spectrum, m/e (relative intensity) 231 (M^+, 62), 230 (80), 212 (46), 162 (100), 69 (19), 42 (30); IR (Nujol) 3450, 3250, 1330, 1220, 1150, 1110, 1055 cm^{-1}.

Anal. Calcd for $C_8H_7NF_6$: C, 41.56; H, 3.03. Found: C, 41.37; H, 3.16.

Registry No. **1a**, 5145-65-3; **1b**, 5044-32-6; **2**, 692-50-2; **3a**, 83248-91-3; **3b**, 83248-92-4; **4**, 83248-93-5; **5a**, 83248-94-6; **5b**, 83248-95-7; **6a**, 83248-96-8; **6b**, 83248-97-9; **7a**, 82912-41-2; **7b**, 83248-98-0.

Nitrogen Bridgehead Compounds. 26.[1] Synthesis and Stereochemistry of 3-Phenylperhydropyrido[1,2-*a*]pyrimidin-4-ones

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4*H*-Pyrido[1,2-*a*]pyrimidin-4-ones possess advantageous pharmacological properties;[2] therefore this class is being extensively investigated.[3] Hitherto, only a few representatives of the perhydro derivatives have been synthesized,[4] and the stereochemistry of these compounds has not been studied. In this paper catalytic hydrogenation of the tetrahydropyridopyrimidines (**1**)[5] and the conformational analysis of the resulting perhydro derivatives are reported.

Synthesis. The hydrogenation was performed in acetic acid solution, in the presence of platinum oxide at 30 °C and under a pressure of 62 atm. Hydrogenation of both **1a** and the 6-methyl derivative **1b** led to mixtures of two diastereoisomeric perhydro derivatives (**2** and **3**, Scheme I). Further diastereoisomers could not be detected by the GC/MS method. The ratio of the diastereoisomers **2** and **3** was 47:53 from **1a** and 40:60 from **1b**, as determined by GC analysis. The diastereomers **2** and **3** were separated

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