distilled under nitrogen from benzophenone ketyl before use.

General Procedure for Coupling of PhYbI with Organic Halides. In a 50-mL centrifuge tube, Yb powder and a magnetic stirring bar were placed under air, and the tube was sealed with a serum cap. After the tube was dried by heating under nitrogen, THF was added by a syringe. Then iodobenzene was added slowly to the tube at −30 °C during 5–10 min. After a short induction period (ca. 10 min), ytterbium started to react with the iodide, and the mixture was further stirred for ca. 2 h at −30 °C. To the resulting red brown THF solution of PhYbI was added the organic halide by syringe at −30 °C. Then the serum cap was removed and the catalysts (10 mol % to Yb) was added all at once to the tube. After the tube was sealed again with a serum cap, the mixture was allowed to warm to room temperature slowly with stirring overnight. The resulting mixture was quenched with 2 N HCl and the products were extracted with ether (5 times). The ethereal layer was treated with saturated NaCl aqueous solution and dried over anhydrous sodium sulfate. After evaporation of the solvent, the products were analyzed by GLC. Considerable amounts of the starting halides were also detected. Identities with the products were performed by NMR and retention time comparison with authentic samples. The results are summarized in Tables I–III.

Coupling Reactions of PhYbI with *cis*- and *trans*-Styryl Bromides. To the THF solution of PhYbI, prepared from Yb (0.5 mmol), PhI (0.75 mmol), and THF (30 mL) as described above, cis-styryl bromide (0.75 mmol) was added by a syringe and then CuBr (0.05 mmol) was added to the mixture at −30 °C. The mixture was allowed to warm slowly to room temperature and stirred overnight. Treatment of the resulting mixture as above gave cis- and trans-stilbenes in 22 and 1% yields, respectively with recovery of the starting cis bromide. Similarly, the reaction with trans-styryl bromide was also carried out to give trans- and cis-stilbenes in 15 and 7% yields, respectively with the unreacted starting bromide.

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Registry No. PhYbI, 26138-28-3; CuI, 7681-65-4; CuBr, 7787-70-4; CuCl, 7758-89-6; $CuCl_2$, 7447-39-4; $Cu(OAc)_2$, 142-71-2; $FeCl_3$, 7705-08-0; $CoCl_2$, 7646-79-9; $PdCl_2$, 7647-10-1; $Pd(PPh_3)_4$, 14221-01-3; $NiCl_2$, 7718-54-9; AgI, 7783-96-2; *n*-BuPh, 104-51-8; PhPh, 92-52-4; *n*-BuI, 542-69-8; PhI, 591-50-4; *n*-BuBr, 109-65-9; $PhCH_2Br$, 28807-97-8; $PhCH_2CH_2Ph$, 103-29-7; *n*-BuCl, 109-69-3; Yb, 7440-64-4; allyl iodide, 556-56-9; allyl bromide, 106-95-6; allyl chloride, 107-05-1; allylbenzene, 300-57-2; *cis*-styryl bromide, 588-73-8; *cis*-stilbene, 645-49-8; *trans*-styryl bromide, 588-72-7; *trans*-stilbene, 103-30-0; *n*-octane, 111-65-9.

A Synthesis of 3-Substituted Pyrroles through the Halogen–Metal Exchange Reaction of 3-Bromo-1-(triisopropylsilyl)pyrrole

Alan P. Kozikowski* and Xue-Min Cheng

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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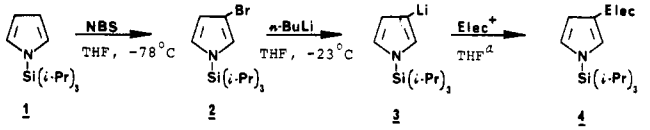
In our efforts to develop new, practical entries to several unique classes of indole-containing natural products, we needed to develop a method for achieving selective functionalization of the β-position of pyrrole. While interaction of pyrrole with an electrophilic agent generally leads to introduction of a new group into its α-position,[1] it has been demonstrated recently that protection of the pyrrole ring nitrogen with a phenylsulfonyl group[2] or the bulky triisopropylsilyl group[3] can lead to substitution at the β-position. Thus, while NBS reacts with the *N*-*tert*-butyldiphenylsilyl derivative of pyrrole to give a mixture of bromopyrroles,[4] the *N*-triisopropylsilyl derivative **1** gives predominantly the corresponding 3-bromo derivative **2**.[3]



We have now shown that 3-bromo-1-(triisopropylsilyl)pyrrole will undergo rapid halogen–metal[5] exchange with *n*-butyllithium in THF to generate the corresponding 3-lithiopyrrole **3**.[6] This anion can be trapped in turn by various electrophiles to provide the corresponding 3-substituted pyrroles **4**. The yields obtained were high in the majority of cases studied (Table I). We believe that the present methodology should find considerable use in the synthesis of compounds of pharmaceutical interest.[7]

Experimental Section

Low-resolution mass spectra were determined on an LKB-9000 instrument. High-resolution mass spectra were determined on a Varian MAT CH-5DF instrument by peak matching. ^1H NMR spectra were recorded at 60 MHz (Varian EM-360) or at 300 MHz (Brüker WH-300). Chemical shifts (δ) are reported downfield from internal Me_4Si. Infrared spectra were obtained on a Perkin-Elmer 247 or 137 spectrophotometer.

3-Bromo-1-(triisopropylsilyl)pyrrole (2). To a solution of 1 (963 mg, 4.32 mmol) in 40 mL of dry THF cooled to −78 °C was added dropwise a solution of *N*-bromosuccinimide (771 mg, 4.33 mmol) in 20 mL of THF. After addition was completed the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure, carbon tetrachloride was added to precipitate the succinimide, and this mixture was filtered. The filter cake was washed with additional carbon tetrachloride, the filtrates were concentrated, and the resulting oil was chromatographed on silica gel to furnish 1.18 g (90%) of **2** as a colorless oil: IR (neat) 2900, 2800, 1470, 1200, 1190, 1075, 910, 880, 765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (dd, 1 H, J = 2.3, 1.4 Hz), 6.67 (dd, 1 H, J = 2.8, 2.4 Hz), 6.29 (dd, 1 H, J = 2.8, 1.4 Hz), 1.43 (heptet, 3 H, J = 7.4 Hz), 1.09 (d, 18 H, J = 7.4 Hz); exact mass calcd for $C_{13}H_{24}{}^{79}BrNSi$ 301.0861, found 301.0862.

3-Allyl-1-(triisopropylsilyl)pyrrole. To a solution of **2** (247 mg, 0.82 mmol) in 10 mL of dry THF cooled to −23 °C (dry ice/CCl_4 bath) was added dropwise 1.1 mL of 1.5 M *n*-butyllithium in hexanes. The reaction mixture was kept at −23 °C for 2 h, and then a solution of allyl bromide (3–4 equiv) in 10 mL of THF was

(1) Jones, R. A.; Bean, G. P. "The Chemistry of Pyrroles"; Academic Press: New York, 1977.

(2) Kakushima, M.; Hamel, P.; Frenette, R.; Rokach, J. *J. Org. Chem.* **1983**, *48*, 3214. Rokach, J.; Hamel, P.; Kakushima, M.; Smith, G. M. *Tetrahedron Lett.* **1981**, *22*, 4901. Xu, R. X.; Anderson, H. J.; Gogan, N. J.; Loader, C. E.; McDonald, R. *Ibid.* **1981**, *22*, 4899.

(3) Muchowski, J. M.; Solas, D. R. *Tetrahedron Lett.* **1983**, *24*, 3455.

(4) A mixture results if the bromination reaction is performed at −78 °C. Bromination at −90 °C, on the other hand, does appear to afford primarily the 3-substituted product, but this bromide rapidly darkens and decomposes upon silica gel chromatography.

(5) Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300.

(6) Interestingly, an attempted halogen–metal exchange reaction on *N*-benzyl-3-bromopyrrole failed using *n*-butyllithium. The reaction was, however, successful with lithium metal, and the resulting β-lithiopyrrole was trapped with carbon dioxide: Anderson, H. J.; Griffiths, S. J. *Can. J. Chem.* **1967**, *45*, 2227. The treatment of *N*-(trimethylsilyl)pyrrole with *tert*-butyllithium followed by carbon dioxide, HCl, and diazomethane affords the 3-carbomethoxy derivative as the major product along with the 1- and 2-mono esters and the 2,5-diester: Chadwick, D. J.; Hodgson, S. T. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1833.

(7) An oxazoline group located at the 2-position of *N*-methylpyrrole has been shown to direct metalation predominantly to the 3-position: Chadwick, D. J.; McKnight, M. V.; Ngochindo, R. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1343.

0022-3263/84/1949-3239$01.50/0

Table I. Reaction of β-Lithiopyrrole 2 with Various Electrophiles

entry	electrophile	yield[b]	^{1}H NMR data ($CDCl_3$) (with exception of the triisopropylsilyl group)	mass spectrum
a	D_2O	quantitative	6.80 (br d, 2 H, J = 1.9 Hz), 6.32 (br d, 1 H, J = 2.0 Hz)	224 (M^+), 181; exact mass calcd for $C_{13}H_{24}DNSi$ 224.1819, found 224.1817
b	MeI	92% + 3% 1	6.69 (narrow t, 1 H), 6.52 (br s, 1 H), 6.14 (narrow t, 1 H), 2.13 (s, 3 H)	237 (M^+), 222, 195, 194; exact mass calcd for $C_{14}H_{27}NSi$ 237.1913, found 237.1908
c	CH_2=$CHCH_2Br$	80% + 13% 1	6.71 (narrow t, 1 H), 6.53 (br s, 1 H) 6.15 (narrow t, 1 H), 6.00 (m, 1 H), 5.02 (m, 2 H), 3.26 (d, 2 H, J = 6.6 Hz)	263 (M^+), 221, 220, 180; exact mass calcd for $C_{16}H_{29}NSi$ 263.2069, found 263.2069
d	PhSSPh	78%	7.12 (m, 5 H), 6.98 (dd, 1 H, J = 2.1, 1.4 Hz), 6.85 (narrow t, 1 H), 6.38 (dd, 1 H, J = 2.5, 1.4 Hz)	331 (M^+), 289, 288, exact mass calcd for $C_{19}H_{29}NSSi$ 331.1790, found 331.1789
e	cyclopentanone	80% (isolated as the cyclopentenyl derivative formed by silica gel promoted dehydration)	6.72 (narrow t, 1 H), 6.70 (br s, 1 H), 6.45 (dd, 1 H, J = 2.7, 1.7 Hz), 5.82 (narrow t, 1 H), 2.60 (m, 2 H), 2.45 (m, 2H), 1.96 (quintet, 2 H)	289 (M^+), 247, 246; exact mass calcd for $C_{18}H_{31}NSi$ 289.2226, found 289.2223
f	PhCHO	70%	7.37 (m, 5 H), 6.72 (narrow t, 1 H), 6.64 (br s, 1 H), 6.20 (m, 1 H), 5.84 (d, 1 H, J = 4.2 Hz), 2.04 (d, 1 H, J = 4.2 Hz	329 (M^+), 222, 180; exact mass calcd for $C_{20}H_{31}NOSi$ 329.2175, found 329.2172
g	$HC(O)NMe_2$	65%	9.84 (s, 1 H), 7.41 (narrow t, 1 H), 6.76 (m, 2 H)	251 (M^+), 209, 208, 180, 166; exact mass calcd for $C_{14}H_{25}NOSi$ 251.1705, found 251.1704
h	PhCOCl	69%	7.85 (m, 2 H), 7.51 (m, 3 H), 7.34 (t, 1 H, J = 1.4 Hz), 6.80 (m, 2 H)	327 (M^+), 285, 284; exact mass calcd for $C_{20}H_{29}NOSi$ 327.2018, found 327.2013

[a] The condensation reactions were carried out at −23 °C for entries a–d and at −78 °C for entries e–h. [b] The products were purified by silica gel chromatography and characterized by ^{1}H NMR, IR, and mass spectral analyses.

added. The reaction mixture was allowed to warm to room temperature over a 20-min period and quenched with 2 mL of water. The mixture was extracted with ether (3×), and the combined extracts were dried ($MgSO_4$) and concentrated. The residue was passed through a short silica gel column to afford 198.4 mg of a mixture of 1 and the title compound (ratio ≃ 1:6).[8] See Table I for spectral data. This mixture was conveniently separated by silica gel chromatography after desilylation (n-$Bu_4N^+F^-$, THF) to provide pure 3-allylpyrrole: ^{1}H NMR ($CDCl_3$) δ 6.75 (m, 1 H), 6.59 (m, 1 H), 6.07 (m, 1 H), 5.99 (m, 1 H), 5.05 (m, 2 H), 3.27 (d, 2 H, J = 6.6 Hz); exact mass calcd for $C_{16}H_{29}NSi$ 263.2069, found 263.2069.

(8) An authentic sample of 2-allylpyrrole was prepared from 1-lithiopyrrole and allyl bromide to further verify that the 3-position is the site of the allylation reaction (Hobbs, C. F.; McMillin, C. K.; Papadopoulos, E. P.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 43. Skell, P. S.; Bean, G. P. *Ibid.* **1962**, *84*, 4655). The ^{1}H NMR spectrum obtained for this compound was substantially different from that obtained for the 3-allylpyrrole prepared by desilylation of 3-allyl-1-(triisopropylsilyl)-pyrrole.

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Registry No. 1, 87630-35-1; 2, 87630-36-2; 4 (Elec = D), 90971-70-3; 4 (Elec = Me), 90971-71-4; 4 (Elec = CH_2=$CHCH_2$), 90971-72-5; 4 (Elec = PhS), 90971-73-6; 4 (Elec = C=$CHCH_2CH_2CH_2$), 90971-74-7; 4 (Elec = PhCH(OH)), 90971-75-8; 4 (Elec = CHO), 90971-76-9; 4 (Elec = PhCO), 90971-77-0; D_2O, 7789-20-0; MeI, 74-88-4; CH_2=$CHCH_2Br$, 106-95-6; PhSSPh, 882-33-7; PhCHO, 100-52-7; $OHCNMe_2$, 68-12-2; PhCOCl, 98-88-4; cyclopentanone, 120-92-3.