orated. The residue was triturated in nm (ε 9100); 731 mg (58%) of 17 as a light green solid, mp 219–221 °C: R_f 0.2, 1:1 EtOAc–hexanes; ^{1}H NMR ($CDCl_3$) δ 1.39 (3 H, t, J = 7), 2.42–2.58 (2 H, m), 3.49–3.67 (4 H, m), 4.37 (2 H, q, J = 7), 4.97 (1 H, bd t), 7.11 (1 H, dd, J = 6 and 11), 8.23 (1 H, dd, J = 9 and 10); IR (KBr) 3040, 2980, 2900, 1710, 1610, 1495, 1300, and 1090 cm^{-1}; UV (EtOAc) λ_{max} = 213 (ε 28 300), 248 (ε 15 800), 257 (ε 17 500), 318 (ε 9800), and 330 nm (ε 9100); MS (m/e) 388, 387, 386, 385, 315 (base), 313. The analytical sample was prepared by recrystallization from MeOH, mp 231–233 °C. Anal. Calcd for $C_{16}H_{14}NO_3F_2Br$: C, 49.76; H, 3.65; N, 3.63. Found: C, 49.64; H, 3.48; N, 3.56.

6 by Dehydrobromination of 17. To a mixture of 2.0 g (5.2 mmol) of 11 and 200 mL of THF containing 1% ethanol was added 0.30 g (5.3 mmol) of KOH (pellets). The suspension was stirred for 3 h at room temperature and then was treated with an additional 0.070 g (1.3 mmol) of KOH. Following additional stirring for 0.5 h, the dark mixture was diluted with 50 mL of 1 N aqueous HCl solution and the THF was removed by rotary evaporation. The aqueous residue was extracted with $CHCl_3$ (200 mL), and the organic layer was backwashed with water (2 × 100 mL), dried ($MgSO_4$), and evaporated to give a tan solid. Recrystallization from EtOAc–hexanes gave 0.75 g (47%) of 6, mp 165–166 °C, which was identical by 300-MHz NMR and TLC to that obtained by thermolysis of 12.

Acknowledgment. We would like to thank Vinod D. Parikh for technical assistance.

Synthesis of 7-Azaindole and 7-Azaoxindole Derivatives through a Palladium-Catalyzed Cross-Coupling Reaction

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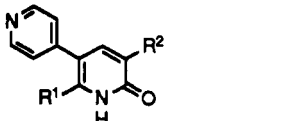
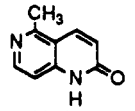
Cardiac glycosides (such as digitalis) have, historically, been used as positive inotropic agents for the treatment of congestive heart failure, a chronic and debilitating disease.[1-3] The search for an orally active non-glycoside inotropic agent displaying a greater safety profile and improved efficacy compared to digitalis resulted in the discovery of a new class of agents, the cAMP phosphodiesterase III inhibitors. These agents comprise a chemically diverse group of compounds including amrinone (1),[4] milrinone (2),[5] medorinone,[6] indolidan, and imazodan.[3,7]

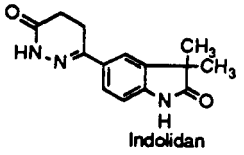


1, R^1 = H, R^2 = NH_2, Amrinone

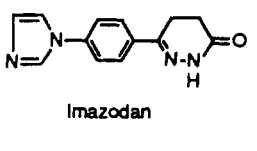
2, R^1 = CH_3, R^2 = CN, Milrinone



Medorinone

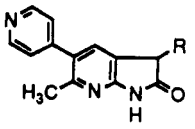


Indolidan



Imazodan

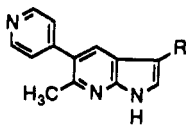
In an effort to improve upon the potency and duration of action of milrinone (2), we have synthesized 7-azaoxindole derivatives (3) (1,3-dihydro-6-methyl-2H-pyrrolo[2,3-b]-pyridin-2-one). These compounds have the essential features that appear to be important for the inotropic activity: a cyclic unsubstituted amide function and an appropriately positioned hydrogen acceptor ring. These structural features were derived from a pharmacophoric analysis of several well-known cardiotonic cAMP phosphodiesterase III inhibitors, primarily milrinone, medorinone, and indolidan. After a similar analysis of several cadiotonic agents, a five-point model for positive inotropic activity has been proposed by Bristol and co-workers.[8]



3

a, R = H

b, R = CH_3



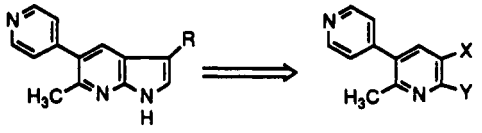
4

a, R = H

b, R = CH_3

Limited general synthetic pathways exist in the literature for the preparation of 7-azaindoles.[9] Taylor[10] and Seitz[11] have recently utilized an intramolecular inverse electron demand Diels–Alder reactions of appropriately substituted 1,2,4-triazines to prepare 7-azaindoles. However, application of this procedure to synthesize more elaborate 7-azaindoles is limited because of the higher temperatures required to effect the Diels–Alder reaction which was often accompanied by the significant decomposition of the starting materials resulting in low yields of the desired products. In addition, substitution of the 1,2,4-triazines further reduces the product yield. We anticipated a similar fate utilizing this Diels–Alder strategy to prepare the above target compounds. Thus we needed a procedure that would provide these fused heterocyclic compounds in good overall yields. We describe, herein, the synthesis of 7-azaoxindole derivatives (3) through the key intermediate, 7-azaindole derivatives 4 (5-(4-pyridinyl)-1H-pyrrolo[2,3-b]pyridines) which in turn were prepared by a palladium-catalyzed cross-coupling reaction of appropriately substituted pyridines.

Retrosynthetic Strategy:



4 8

The general application of palladium-catalyzed cross-coupling reactions has provided new avenues to obtain key synthetic intermediates for the preparation of condensed heteroaromatic compounds that were inaccessible through

† Deceased.

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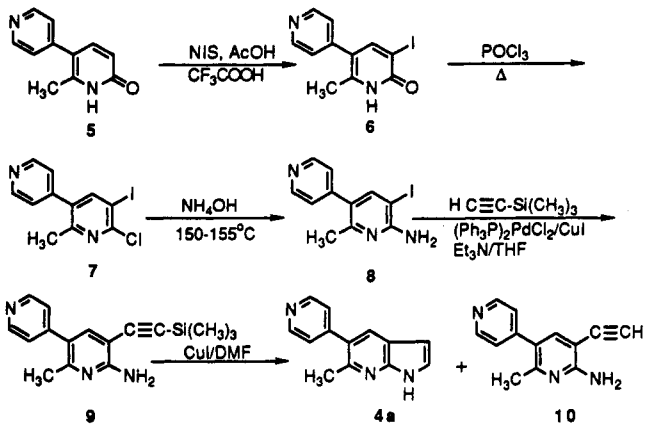
Scheme I



the classical methods. This methodology has been extensively used for the synthesis of various substituted indoles.[12] Application of this procedure for the synthesis of azaindole derivatives has not been investigated in detail except for the preparation of the isomeric 4-azaindoles.[12] Our synthetic strategy to prepare 7-azaindole derivatives **4(a and b)** was also based on palladium-catalyzed carbon–carbon bond formation as a key synthetic step from the appropriately ortho-functionalized pyridine **8** (for example: X = I, Y = NH_2; Scheme I).

The requisite intermediate **8** was prepared as described in Scheme I. Hydrolysis and decarboxylation of milrinone (**2**) with 85% H_2SO_4 gave **5**[13] in 75% yield. Iodination of **5** with *N*-iodosuccinimide in AcOH in the presence of a catalytic amount of CF_3CO_2H afforded the 3-iodobipyridine derivative **6** in 93% yield. Refluxing **6** in excess of $POCl_3$ gave 2-chloro-3-iodobipyridine (**7**) (72% yield) that was then converted to intermediate **8** (89% yield) by heating in a mixture of ethanol and 28% aqueous NH_4OH in a stirred Parr apparatus at 150–155 °C. The palladium-catalyzed coupling reaction of **8** with (trimethylsilyl)acetylene resulted in **9** in 96% yield. Cyclization of **9** was accomplished with CuI in refluxing DMF[14] to give the 7-azaindole derivative **4a** in 40% yield after chromatography. Proteodesilylation also occurred either during the course of reaction or workup. In addition a significant amount of **10** (35% yield) was obtained as a result of proteodisilylation either during the reaction or workup of the starting material. The structural assignment of **10** was made on the basis of ^1H NMR and MS spectra. Various attempts including the use of $NaNH_2/DMF$[14] failed to improve the yield of the desired compound **4a**; thus we needed an alternative pathway which was amenable to scaleup.

We explored Suzuki's method[15] for the preparation of indoles through a palladium-catalyzed borane coupling reaction to synthesize 7-azaindoles. (2-Ethoxyvinyl)boranes **11** were prepared by the addition of catecholborane to the corresponding ethoxyacetylenes in quantitative yields following the reported procedures[15] and were used directly in the next reaction without any purification. Reaction of the boranes **11** with **5** (Scheme II) in the presence of catalytic amounts of $(Ph_3P)_4Pd$ in THF and powdered NaOH provided vinyl ethers **12** which without isolation were treated with 2 N HCl for 48 h to give the desired 7-azaindoles (**4a**, 78%; **4b**, 40%; isolated yields) after basic workup. The slower reaction of the sterically hindered vinyl borane **11** (R = CH_3) with **8** during the palladium-catalyzed coupling reaction may have contributed to the lower yield of **4b**. Protection of the amino group was not necessary for either of the above procedures.

Oxidative bromination of 7-azaindoles **4** (**a** and **b**) with Br_2/48% HBr in an aqueous medium or with pyridinium-bromide perbromide in *t*-BuOH[16] resulted in the corresponding 3,3-dibromo-7-azaoxindoles (R = H) and 3-bromo-7-azaoxindole (R = CH_3) (Scheme III). Without any further purification, the crude bromo compounds were reduced with excess Zn/AcOH to give the 7-azaoxindoles (**3a**, 71%; **3b**, 65% isolated yields).

In summary, the procedure reported herein is a general and efficient synthesis of 7-azaindoles from appropriately functionalized pyridines through palladium-catalyzed cross-coupling reactions. The corresponding 7-azaoxindoles were also prepared in good yields by reduction of the intermediate 3,3-dibromo-(or 3-bromo)-7-azaoxindoles with Zn/AcOH.

Experimental Section

Melting points were taken using a Mel Temp apparatus and are uncorrected. ^1H NMR spectra were recorded on a Varian Model HA-100, Bruker-AC 200, and GE QE-300 (300 MHz) spectrometer with tetramethylsilane as an internal standard. IR spectra were obtained on a Perkin-Elmer Model 21 spectrometer. Mass spectra were determined using a Jeolco JMS-OISC Model instrument. TLC was performed on E. Merck 5- × 20-cm Kiselgel 60F-254 plates. Column chromatography was performed with 60–200-mm silica gel 60 (EM reagent).

5-Iodo-2-methyl[3,4′-bipyridyl]-6(1*H*)-one (6). To a stirred solution of bipyridone **5**[13] (14.0 g, 0.075 mol) in AcOH (140 mL) at rt under a N_2 atmosphere was added CF_3CO_2H (7 mL) followed by *N*-iodosuccinimide (16.87 g, 0.075 mol), and the mixture was stirred for 18 h. The reaction mixture was then poured into ice–water and neutralized with 28% aqueous NH_4OH. The resulting solid was filtered, dried, and recrystallized from CH_3CN to give **6**, 17.2 g (73%), as a pale yellow solid: mp 235–238 °C dec; IR (KBr) 3050, 1635, 1585 cm^{-1}; MS (CI) MH^+ 313; ^1H NMR (DMSO-d_6, 200 MHz) δ 2.15 (s, 3 H), 7.34 (d, J = 4.5 Hz, 2 H), 8.05 (s, 1 H), 8.60 (d, J = 4.0 Hz, 2 H), 12.15 (bs, 1 H).

Anal. Calcd for $C_{11}H_9IN_2O$: C, 42.33; H, 2.91; N, 8.98; I, 40.66. Found: C, 42.67; H, 3.02; N, 8.89; I, 40.46.

6-Chloro-5-iodo-2-methyl-3,4′-bipyridyl (7). To a suspension of **6** (11.6 g, 0.037 mol) in $POCl_3$ (100 mL) was added DMF (2 mL), and the reaction mixture was heated to reflux with stirring for 4 h. After removal of excess $POCl_3$ by distillation at atmospheric pressure, the residue was poured into ice–water and neutralized with 28% aqueous NH_4OH solution. The product was then extracted with CH_2Cl_2 (3 × 100 mL), dried over anhyd $MgSO_4$, and evaporated to dryness to give a brown gum. The crude product was purified by passing through a pad of silica gel (CH_2Cl_2–ether, 4:1), and recrystallization from EtOAc gave **7**, 8.1 g (72%), as a light yellow solid: mp 149–151 °C; IR (KBr) 3460, 3320, 1600, 1410 cm^{-1}; MS (CI) MH^+ 331; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.48 (s, 3 H), 7.25 (d, J = 4.4 Hz, 2 H), 7.95 (s, 1 H), 8.75 (d, J = 4.5 Hz, 2H).

Anal. Calcd for $C_{11}H_8ClIN_2$: C, 39.97; H, 2.44; N, 8.47; Cl, 10.73. Found: C, 39.72; H, 2.31; N, 8.39; Cl, 10.39.

6-Amino-5-iodo-2-methyl-3,4′-bipyridyl (8). A suspension of **7** (5.0 g, 0.15 mol) in EtOH (50 mL) and 28% aqueous NH_4OH (150 mL) was heated in a Parr apparatus (600-mL size) equipped with stirrer at 150–155 °C for 18 h. The reaction mixture was cooled to rt, and the resulting suspension was evaporated to dryness to give crude **8**. Recrystallization from EtOAc gave **8**, 4.2 g (89%), as a beige solid: mp 179–181 °C; IR (KBr) 3420, 3180,

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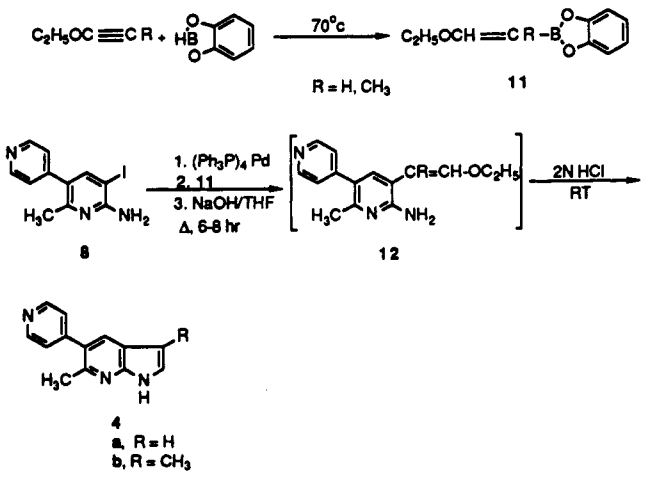
Scheme II



1630, 1580, 1455 cm^{-1}; MS (CI) MH^+ 312; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.35 (s, 3 H), 5.05 (bs, 2 H), 7.20 (d, J = 4.0 Hz, 2 H), 7.74 (s, 1 H), 8.62 (d, J = 4.4 Hz, 2 H).

Anal. Calcd for $C_{11}H_{10}IN_3 \cdot 0.25H_2O$: C, 41.86; H, 3.35; N, 13.31. Found: C, 41.73; H, 3.44; N, 13.12.

6-Amino-5-[(trimethylsilyl)ethynyl]-2-methyl-3,4′-bipyridyl (9). To a solution of 8 (6.22 g, 20 mmol) in Et_3N (120 mL) and THF (20 mL) under an argon atmosphere was added $(Ph_3P)_2PdCl_2$ (0.14 g, 0.2 mmol) and CuI (0.038 g, 0.2 mmol) followed by (trimethylsilyl)acetylene (2.94 g, 30 mmol). The reaction mixture was stirred at rt for 18 h, and the solvent was removed under reduced pressure. Purification of the residue on a silica gel column (EtOAc–ether, 1:1) gave a solid which was recrystallized from ether–hexane (1:1) to give 9, 5.2 g (96%), as a cream-colored solid: mp 173–175 °C; IR (KBr) 3320, 3160, 2140, 1640, 1460, 1225 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.26 (s, 9 H), 2.40 (s, 3 H), 5.15 (bs, 2 H), 7.20 (bs, 2 H), 7.45 (s, 1 H), 8.65 (bs, 2 H).

Anal. Calcd for $C_{16}H_{19}N_3Si \cdot 0.25H_2O$: C, 67.25; H, 6.83; N, 14.71; Si, 9.80. Found: C, 67.43; H, 6.79; N, 14.30; Si, 9.95.

6-Methyl-5-(4-pyridinyl)-1*H*-pyrrolo[2,3-*b*]pyridine (4a) and 6-Amino-5-ethynyl-2-methyl-3,4′-bipyridyl (10). To a solution of 9 (3.0 g, 10.64 mmol) in dry DMF (100 mL) under an argon atmosphere was added CuI (0.02 g, 0.104 mmol), and the reaction mixture was heated to reflux for 6 h. After the mixture was cooled to rt, the solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2, washed with 28% aqueous NH_4OH, dried over $MgSO_4$, and evaporated to dryness to give the crude products. Silica gel column chromatography (CH_2Cl_2–CH_3OH, 20:1) gave the first product which was recrystallized from EtOAc to give 4a, 0.9 g (40%), as a white solid: mp 251–253 °C; IR (KBr) 3120, 3060, 1600, 1400, 1280 cm^{-1}; MS (CI) MH^+ 211; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.64 (s, 3 H), 6.51 (bd, J = 2.5 Hz, 1 H), 7.32 (d, J = 5.5 Hz, 2 H), 7.36 (m, 1 H), 7.80 (s, 1 H), 8.70 (d, J = 5.0 Hz, 2 H).

Anal. Calcd for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.24; H, 5.19; N, 20.13.

The second product was eluted from the column using CH_2Cl_2–CH_3OH (9:1) and recrystallized from THF to give 10, 0.78 (35%), as a white solid: mp 189–190 °C; IR (KBr) 3270, 3180, 2100, 1640, 1600, 1460 cm^{-1}; MS (CI) MH^+ 211; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.28 (s, 3 H), 3.40 (s, 1 H), 5.18 (bs, 2 H), 7.10 (d, J = 5.2 Hz, 2 H), 7.24 (s, 1 H), 8.64 (d, J = 5.1 Hz, 2 H).

Anal. Calcd for $C_{13}H_{11}N_3 \cdot 0.5H_2O$: C, 71.56; H, 5.75; N, 19.26. Found: C, 71.15; H, 5.81; N, 19.04.

Alternative Synthesis of 6-Methyl-5-(4-pyridinyl)-1*H*-pyrrolo[2,3-*b*]pyridine (4a). To a solution of 50% ethoxyacetylene in hexane (11.5 g, 81 mmol) under an argon atmosphere at 0–5 °C was added catecholborane (8.74 g, 73 mmol) dropwise. The mixture was then stirred at rt for 2 h followed by heating at 70 °C for another 2 h. The reaction mixture was then cooled to rt, and to the dark solution were sequentially added 8 (13.0 g, 42.12 mmol) in dry THF (170mL), tetrakis(triphenylphosphine)palladium (1.5 g, 9.6 mmol), and powdered NaOH (5.1 g, 126.36 mmol). The reaction mixture was heated to reflux with stirring for 8 h, cooled to rt, and then treated with 2 N HCl (150 mL). Stirring was continued at rt for 48 h, and then the solvent (THF) was removed under reduced pressure. The residual aqueous solution was filtered through a Celite pad and extracted with ether, and the ether layer was discarded. The aqueous layer was then cooled in an ice bath and neutralized with 5 N NaOH solution to give a beige solid. The solid was filtered, washed with water, and dried. Recrystallization from EtOAc gave 4a (6.8 g, 78%) as a white solid. The compound displayed identical IR, MS, and ^1H NMR spectra compared to the product obtained by the procedure described above.

3,6-Dimethyl-5-(4-pyridinyl)-1*H*-pyrrolo[2,3-*b*]pyridine (4b). This was prepared from ethoxypropyne following the above procedure in 40% yield: mp 240–242 °C; IR (KBr) 3110, 2880, 1600, 1580, 1420, 1280 cm^{-1}; MS (CI) MH^+ 224; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.16 (s, 3 H), 2.60 (s, 3 H), 7.10 (s, 1 H), 7.38 (d, J = 4.5 Hz, 2 H), 7.76 (s, 1 H), 8.70 (d, J = 4.8 Hz), 10.30 (bs, 1 H).

Anal. Calcd for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 74.92; H, 5.78; N, 18.69.

1,3-Dihydro-6-methyl-5-(4-pyridinyl)-2*H*-pyrrolo[2,3-*b*]-pyridin-2-one (3a). To a suspension of 4a (3.0 g, 14.33 mmol) in H_2O (15 mL) was added 48% aqueous HBr (0.5 mL), and the resulting solution was cooled to 0–5 °C. Bromine (6.7 g, 43.06 mmol) was added dropwise, and the solution was stirred at 5 °C for 15 min and then at rt for 30 min.

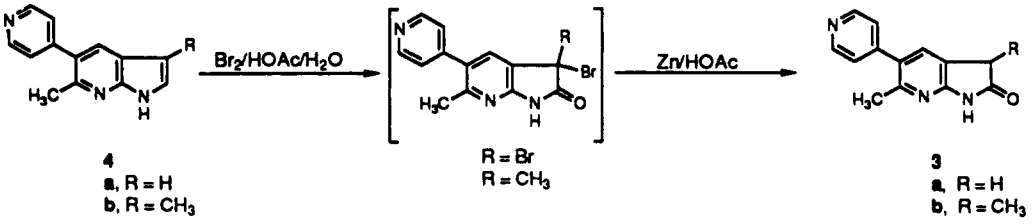
After addition of AcOH (200 mL) and zinc dust (15.0 g, 229.46 mmol) to the above reaction mixture, the resulting suspension was stirred at rt for 1.5 h. The reaction mixture was then filtered through a Celite pad, and the filtrate was evaporated to dryness to give an oil. The oil was dissolved in 2 N HCl (25 mL), and the pH of the solution was adjusted to 9.0 with 5 N NaOH at 0 °C. The resulting solid was filtered, dried-, and recrystallized from DMF–H_2O (1:1) to give 3a, 2.3 g (71%), as a light pink solid: mp 289–291 °C dec; IR (KBr) 3107, 3082, 3019, 2796, 1712, 1628, 1596, 1477, 1225 cm^{-1}; MS (CI) MH^+ 226: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3 H), 3.98 (s, 2 H), 7.25 (d, J = 4.5 Hz, 2 H), 7.38 (s, 1 H), 8.70 (d, J = 4.4 Hz, 2 H), 9.50 (bs, 1 H).

Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.65. Found: C, 69.00; H, 4.75; N, 18.45.

1,3-Dihydro-3,6-dimethyl-5-(4-pyridinyl)-2*H*-pyrrolo[2,3-*b*]pyridin-2-one (3b). Compound 3b was prepared from 4b following the above procedure in 65% yield as a light yellow solid: mp 248–250 °C; IR (KBr) 3564, 3129, 2978, 1719, 1614, 1465, 1216 cm^{-1}; MS (CI) MH^+ 240; ^1H NMR (DMSO-d_6, 300 MHz) δ 1.38 (d, J = 6.5 Hz, 3 H), 3.30 (s, 3 H), 3.50 (q, J = 3.5 Hz; J = 5.8 Hz, 1 H), 7.42 (d, J = 4.5 Hz, 2 H), 7.58 (s, 1 H), 8.60 (d, J = 4.6 Hz, 2 H).

Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56. Found: C, 70.22; H, 5.53; N, 17.47.

Scheme III



Acknowledgment. We are grateful to Dr. Malcolm R. Bell for helpful discussions during the course of this work. We would like to thank the Department of Molecular Characterization for the IR, NMR, and MS spectra.

Economical and Convenient Synthesis of *p*-Ethynylbenzoic Acid and *p*-Ethynylbenzoyl Chloride

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Department of Macromolecular Science, Case Western Reserve University, Cleveland, Ohio 44106

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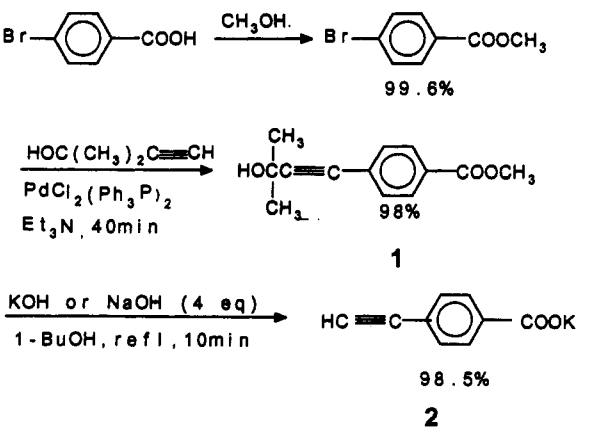
Five methods[1-8] have been reported for the synthesis of *m*- and *p*-ethynylbenzoic acids in yields varying from poor to moderate (26–59%). These methods require isolation and/or purification of intermediates and are cumbersome and costly to perform on a large scale.

The most important procedure for the synthesis of *p*-ethynylbenzoic acid (EBA) (and *p*-ethynylbenzoyl chloride (EBC) from EBA)[5-8] involves coupling of methyl *p*-bromobenzoate with (trimethylsilyl)acetylene in the presence of palladium(0) complexes to give the (trimethylsilyl)ethynylated intermediate, followed by a two-step deprotection and hydrolysis. Because of the high cost of the (trimethylsilyl)acetylene, this method has been limited to laboratory preparations.

2-Methyl-3-butyn-2-ol (MEBYNOL) has been used by other investigators for synthesizing acetylene-terminated derivatives[9-14] including ethynyl benzoic acid esters[3,12] because of its very low cost. Sabourin and Onopchenko[9] reported a convenient synthesis of 4-ethynylphthalic acid (anhydride) via MEBYNOL. Havens and Hergenrother[12] reported the synthesis of several arylacetylenes from 4-aryl-2-methyl-3-butyn-2-ols using sodium hydride as the base for deprotection. Shvartsberg and Moroz[3] synthesized *o*-, *m*-, and *p*-ethynylbenzoic acid esters by deprotecting $EtOCHMeOCMe_2CCC_6H_4CO_2Me$ in 27% total yield.

These methods[1-8,12] have not been used for large-scale syntheses because the yields were low. Coupling of methyl *p*-bromobenzoate with (trimethylsilyl)acetylene[5-8] and subsequent deprotection, although expensive,[12,15] is the present method of choice.[16] Because of the high cost of (trimethylsilyl)acetylene, we decided to develop a high-yield synthetic route to EBA using the very cheap reagent, MEBYNOL.

Scheme I. Synthetic Route to *p*-Ethynylbenzoic Acid



Results and Discussion

A modified synthetic route to EBA and EBC was developed which is much cheaper and faster than previous methods and gives essentially quantitative yields (Scheme I). We took advantage of the sensitivity of the ester linkage toward potassium or sodium hydroxide to cleave the 2-hydroxypropyl group and saponify the ester simultaneously in 1-butanol or 2-propanol to prepare EBA in high yield.

Methyl *p*-bromobenzoate (MBB) was coupled with 2-methyl-3-butyn-2-ol (MEBYNOL) using Pd(0)/CuI catalysis to give the intermediate. 4-(4-(methoxycarbonyl)-phenyl)-2-methyl-3-butyn-2-ol (1) in 98% yield with 99% purity. MBB was mixed with a small excess of MEBYNOL in deaerated, dried triethylamine/pyridine (volume ratio 5/2) in the presence of catalytic amounts of dichlorobis(triphenylphosphine)palladium, triphenylphosphine, and cuprous iodide, and the solution was refluxed. The reaction was complete in 40 min. The isolated intermediate was hydrolyzed and deprotected by refluxing in 1-butanol (10 min) or 2-propanol (2 h) using an excess of sodium or potassium hydroxide. The sodium or potassium salt of EBA precipitated quantitatively from the solution as it was formed (98.5% yield), with 99% purity.

EBA was obtained by acidifying an aqueous solution of the potassium or sodium salt to pH 2.5. It precipitated quantitatively as a white solid of 99% purity.

Crystalline EBA changes color from white to off-white on standing and then to light tan. Its GPC just after isolation shows a sharp single peak; the GPC of the off-white sample shows a slight broadening, which broadens more for the light tan sample. Based on the GPC changes, we postulate that EBA polymerizes slowly at room temperature. However, its sodium and potassium salts are stable.

The high yield in deprotection is probably obtained because while the dimethylethynylcarbinol salt is partially soluble in the alcohol, the deprotected salt precipitates quantitatively as it is formed. It is therefore protected against further attack by the base.

Ethynylbenzoyl chloride (EBC) was prepared in 99% yield and 99% purity by stirring either EBA or its salt with an excess of thionyl chloride in chloroform.

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