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Synthesis of 1-Phenyl-3-(pyridine-4-yl)prop-2-ynyl Acetate

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The propargyl alcohol (**3**) was synthesized by the treatment of benzaldehyde (**1**) with trimethylsilylacetylene and *n*-butyl lithium in THF at -78ºC. After removing of trimethylsilyl with KOH in MeOH, 1-phenylprop-2-yn-1-ol (**4**) was obtained. The coupling of this compound **4** with 4-bromopyridine yielded the 1-phenyl-3-(pyridin-4-yl)prop-2-yn-1-ol (**5**) which was converted to acetate **6** *via* acetic anhydride.

Key Words: Coupling reaction, 1-Phenyl-3-(pyridine-4-yl)prop-2-ynyl acetate.

INTRODUCTION

The chemistry of acetylene substituted molecules has gained increasing attention due to their use in construction of carbon rich scaffold[1], supramolecular system[2], molecular materials[3], nanoelectronic architectures[4], liquid crystalline matter[5]. The carbon-carbon bond forming reactions are among the most powerful methods in organic synthesis and play a crucial role in modern materials[6] science and medicinal chemistry[7]. Herein, the synthesis of the 1-phenyl-3-(pyridine-4-yl)prop-2-ynyl acetate *via* Sonogashira coupling[8] reaction is reported. This compound is the precursor for synthetically and pharmaceutically valuable materials as well as the starting material of allenes[9].

EXPERIMENTAL

3-(Trimethylsilyl)-1-phenylprop-2-yn-1-ol 3[10,11]: To a solution of (trimethylsilyl)acetylene (2.89 g, 4.4 mL, 29.5 mmol) in THF (20 mL) at -78ºC was added *n*-BuLi (1.6 M, 17.7 mL, 28.3 mmol) under the nitrogen. The reaction mixture was slowly warmed (1 h) to -10ºC, then benzaldehyde (2.50 g, 2.30 mL, 23.6 mmol) in THF (5.0 mL) was added slowly *via* syringe. After being stirred for further 1h the mixture was washed with saturated NH_4Cl and organic layer was washed with brine (2 × 20 mL), dried over $MgSO_4$, concentrated under vacuum to yield the desired compound (4.8 g, 100 %) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$), δ = 0.24 (s, 9H), 3.10 (brs, 1H), 5.44 (s, 1H), 7.32-7.40 (m, 3H), 7.53-7.56

(m, 2H); ^{13}C (100 MHz, $CDCl_3$), δ = -0.27, 64.6, 91.2, 105.2, 126.6, 128.1, 128.4, 140.3.

1-Phenylprop-2-yn-1-ol 4[11]: A solution of 1-phenyl-3-trimethylsilyl-prop-2-yn-1-ol (4.52 g, 22.1 mmol) in MeOH (10.0 mL) was treated with finely powdered KOH (1.8 g, 33.2 mmol) in MeOH (5.0 mL). The reaction was completed for 3 h at room temperature. It was acidified 1 N HCl. The aqueous solution was separated and neutralized with aqueous K_2CO_3 and extracted with diethyl ether (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under vacuum to give the product (2.4 g, 82 %) as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$), δ = 2.69 (d, J = 2.0 Hz, 1H), 4.23 (brs, 1H), 5.44 (d, J = 3.2 Hz, 1H), 7.33-7.42 (m, 3H), 7.56-7.58 (m, 2H); ^{13}C (100 MHz, $CDCl_3$), δ = 64.2, 75.0, 84.0, 126.9, 128.5, 128.8, 140.5.

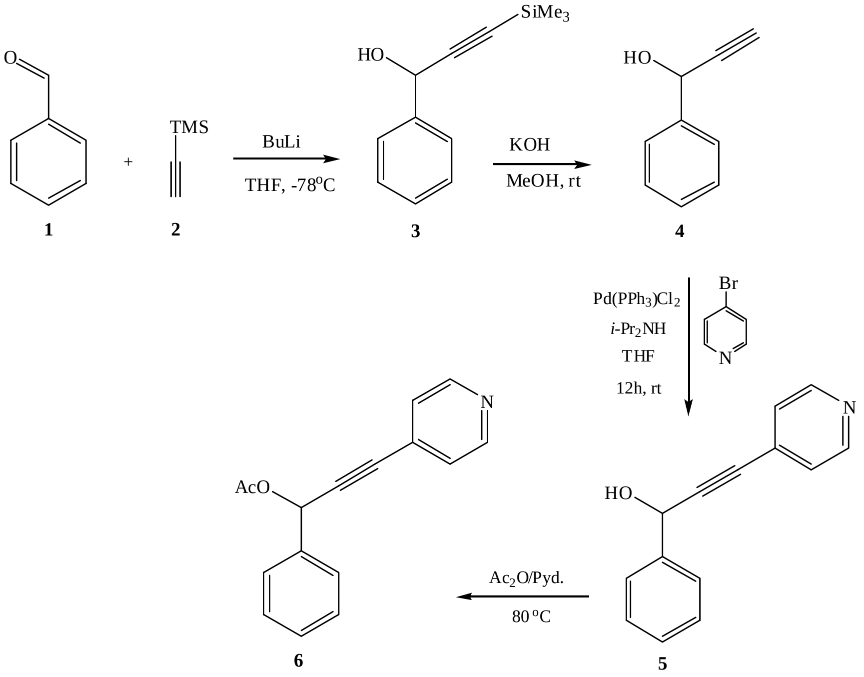
1-Phenyl-3-(pyridine-4-yl)prop-2-yn-1-ol 5[12]: To a solution of 4-bromopyridine hydrochloride (1.76 g, 9.04 mmol) and 1-phenylprop-2-yn-1-ol (1.50 g, 11.3 mmol) in the mixture of THF-diisopropylamine (25 mL, 2/1) were added bis(triphenylphosphine)palladium chloride (79 mg, 0.113 mmol) and copper (1) chloride (86 mg, 0.452 mmol) and the mixture was stirred for 5 h at ambient temperature. The reaction mixture was washed with water (10.0 mL) and the product was extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was dried over $MgSO_4$. After filtration and evaporation of the solvent, the crude material was purified by column chromatography on silica, using gradient elution with hexane and EtOAc. Elution with a 1:1 ratio of solvents afforded the product (0.47 g, 20%) as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$), δ = 5.20 (brs, 1H), 5.69 (s, 1H), 7.22 (d, J = 6.0 Hz, 2H), 7.33-7.38 (m, 3H), 7.58 (m, 2H), 8.37 (d, J = 6.0 Hz, 2H); ^{13}C (100 MHz, $CDCl_3$), δ = 64.5, 83.1, 95.3, 126.0, 126.8, 128.5, 128.8, 131.6, 140.6, 149.1; UV-Vis (CH_2Cl_2), λ_{max} (ε) = 247 (13400 M^{-1} cm^{-1}); ms (FAB^+): m/z 210 [M + H^+].

1-Phenyl-3-(pyridine-4-yl)prop-2-ynyl acetate (6): The 1-phenyl-3-(pyridine-4-yl)prop-2-yn-1-ol (0.13 g, 0.62 mmol) in Ac_2O (2.0 mL) and 2 drops of pyridine was heated at 80ºC for 0.5 h, allowed to stand 0.5 h at room temperature. The reaction mixture was washed with water (10 mL) and the product was extracted with CH_2Cl_2 (3 × 15 mL), dried over $MgSO_4$, after filtration and evaporation of the solvent, the crude material was chromatographed on silica gel (hexane:EtOAc, 4:1) to give the product (62 mg, 40 %) as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$), δ = 2.11 (s, 3H), 6.65 (s, 1H), 7.30-7.41 (m, 5H), 7.54 (m, 2H), 8.57 (brs, 2H); ^{13}C (100 MHz, $CDCl_3$), δ = 20.9, 65.6, 84.1, 90.3, 125.8, 127.7, 128.8, 129.2, 130.3, 136.3, 149.6, 169.6; IR (CH_2Cl_2), ν = 955, 1066, 1347, 1371, 1415, 1456, 1495, 1540, 1594, 1738, 2230, 2258, 2855, 2928, 3037 cm^{-1}; UV-Vis (CH_2Cl_2), λ_{max} (ε) = 240 (15300 M^{-1} cm^{-1}); ms (FAB^+), m/z (%): 252 [M +

H^+] (100), 210 (22), 192 (45), 173 (35), 109 (65); elemental analysis % Calcd. (found) for $C_{16}H_{13}NO_2$ (251.3) : C 76.48 (76.42), H 5.21 (5.25), N 5.57 (5.53).

RESULTS AND DISCUSSION

The propargyl alcohol (**3**) was synthesized by treating of benzaldehyde (**1**) with trimethylsilylacetylene and *n*-butyl lithium in THF. Removal of the silyl group was performed with potassium hydroxide in methanol to give the 1-phenyl-2-propyn-1-ol (**4**). The coupling of alkyne **4** with bromopyridine afforded the pyridine derivative of benzene **5** converted to acetate **6** with acetic anhydride in presence of pyridine at room temperature. The characteristic signals for ^{1}H NMR spectrum are the methyl, resonating at 2.11 as a singlet and propargl proton, resonating at 6.65 as a singlet. Twelve lines ^{13}C NMR spectra are also in agreement with the proposed structure.



REFERENCES

1. R.E. Martin and F. Diederich, *Angew. Chem. Int. Ed.*, **38**, 1350 (1999); U.H.F. Bunz, *Chem. Rev.*, **100**, 1065 (2000); *Acc. Chem. Rev.*, **34**, 998 (2001).
2. F.M. Romero, R. Ziessel, A. Dupont-Gervias and A. Van Dorsselaer, *Chem. Commun.*, 551 (1996); J.A. Whiteford, C.V. Lu and P.J. Stang, *J. Am. Chem. Soc.*, **119**, 2524 (1997); S. Yamazaki, A.J. Deeming, D.M. Speel, D.E. Hibbs, M.B. Hursthouse and K.M.A. Malik, *Chem. Commun.*, 177 (1997).

3. J.J. Wolf, F. Siegler, R. Matschiner and R. Wortmann, *Angew. Chem., Int. Ed.*, **39**, 1436 (2000); B.R. Cho, S.J. Lee, S.H. Lee, K.H. Son, Y.H. Kim, J.-Y. Doo, G.J. Lee, T.I. Kang, Y.K. Lee, M. Cho and S.-J. Jeon, *Chem. Mater.*, **13**, 1438 (2001); J.G. Rodriguez, J. Esquivias, A. Lafuente and C. Diaz, *J. Org. Chem.*, **68**, 8120 (2003).
4. J.M. Tour, *Acc. Chem. Res.*, **3**, 791 (2000); J.M. Tour, L. Chang, D. Nackashi, Y. Yao, A.K. Flatt, S.K.S. Angelo, T.E. Mallouk and P.D. Franzon, *J. Am. Chem. Soc.*, **125**, 13279 (2003).
5. K. Pieterse, A. Lauritsen, A.P.H.J. Schenning, J.A.J.M. Vekemans and E.W. Meijer, *Chem. Eur. J.*, **9**, 5597 (2003); M. Fischer, G. Lieser, A. Rapp, I. Schnell, W. Mamdough, S. De Feyter, F.C. Schryver and S. Hoger, *J. Am. Chem. Soc.*, **126**, 214 (2004); J. Wu, M.D. Watson, L. Zhang, Z. Wang and K. Mullen, *J. Am. Chem. Soc.*, **126**, 177 (2004).
6. P. Bordat and R. Brown, *Chem. Phys. Lett.*, **331**, 439 (2000).
7. A. Zapf and M. Beller, *Top. Catal.*, **19**, 101 (2002); J.G. de Varies, *Can. J. Chem.*, **79**, 1086 (2001); A.C. Hiller, G.A. Grassa, M.S. Viciu, H.M. Lee, C. Yang and S.P. Nolan, *J. Organomet. Chem.*, 653 (2002); U. Beutler, J. Mazacek, G. Penn, B. Schenkel and D. Wasmuth, *Chimica*, **50**, 154 (1996); G.A. Grassa, M.S. Viciu, J. Huang, C. Zhang, M.L. Trudell and S.P. Nolan, *Organometallics*, **21**, 2866 (2002); G.B. Smith, G.C. Dezeny, D.L. Hughes, A.O. King and T.R. Verhoeven, *J. Org. Chem.*, **59**, 8151 (1994).
8. K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, **16**, 4467 (1975); K. Takahashi, Y. Kuroyama and K. Sonogashira, *Synthesis*, 627 (1980).
9. T. Tabuchi, J. Inanaga and M. Yamaguchi, *Tetrahedron Lett.*, **27**, 5237 (1986); J. Inanaga, Y. Sugimoto and T. Hanamoto, *Tetrahedron Lett.*, **33**, 7035 (1992).
10. H. Yamabe, A. Mizuno, H. Kusama and N. Iwasawa, *J. Am. Chem. Soc.*, **127**, 3248 (2005).
11. T. Mukaiyama, K. Suzuki, K. Soal and T. Sato, *Chem. Lett.*, 447 (1979).
12. M.L. Edwards, D.M. Stemerick, J.S. Sabol, K.A. Diekema and R.J. Dinerstein, *J. Med. Chem.*, **37**, 4357 (1994).

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