Pergamon

Tetrahedron Letters 43 (2002) 6697–6700

TETRAHEDRON LETTERS

Synthesis of oligo(2-ethynylpyridines): novel building blocks for supramolecular systems

Tomikazu Kawano,* Takahiro Kato, Chong-Xu Du and Ikuo Ueda*

The Institute of Scientific and Industrial Research, Osaka University, 8-1 Mihogaoka, Ibaraki, Osaka 567-0047, Japan

Received 1 July 2002; revised 25 July 2002; accepted 26 July 2002

Abstract—New oligo(2-ethynylpyridines) **1** are synthesized as novel building blocks for the construction of supramolecular systems by the coupling reaction of the novel dibromopyridines **2** with ethynylpyridines **3**.

Oligopyridines have received considerable attention as versatile building blocks for the construction of supramolecular systems.[1] We recently reported the syntheses and complexation studies of 2-ethynylpyridine ligands.[2–4] Continuing our investigations on 2-ethynylpyridine ligands, we planned to prepare new oligopyridine systems in which the pyridine rings are separated from each other by ethynyl spacers. Metal complexes derived from these new oligopyridines would be expected to possess potential applications in material, molecular and polymer science. Although there have been many reports on the acetylenic-bridged oligo(bi- or terpyridines)[5] and the simple 2-ethynylpyridines such as bis(2-pyridyl)acetylenes,[6] no oligo(2-ethynylpyridines) having more than four pyridine rings have been documented in the literature.[7] This may be explained by the lack of a suitable synthetic route to such higher oligopyridines. Herein, we report a facile synthesis of new oligo(2-ethynylpyridines) **1** by using dibromopyridine derivatives **2**[8] and ethynylpyridine derivatives **3**, both of which are novel key intermediates (Fig. 1).

Scheme 1 shows the synthesis of dibromopyridine derivative **2b**. Treatment of 2-bromo-6-(hydroxymethyl)pyridine **4**,[9,10] which was prepared from commercially available 2,6-dibromopyridine **2a**, with methanesulfonyl chloride (MsCl) in tetrahydrofuran (THF) at −40°C, followed by displacement of the resulting mesylate with iodide ion in acetone at 60°C gave the corresponding primary iodide **5** in 93% yield from **4**. Arbuzov reaction of **5** with triethyl phosphite at

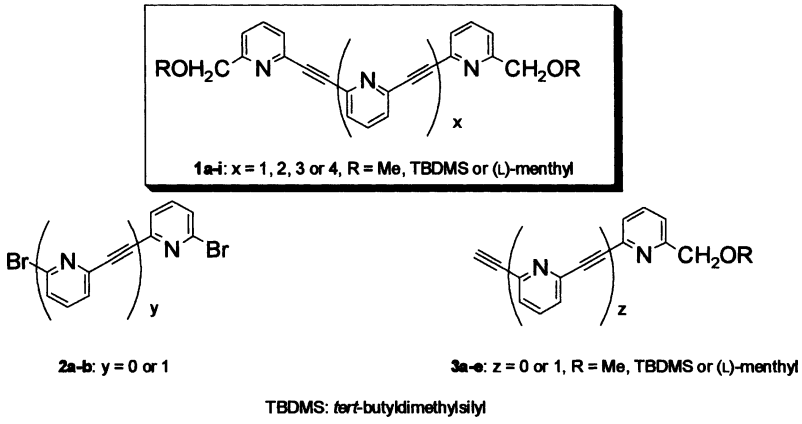
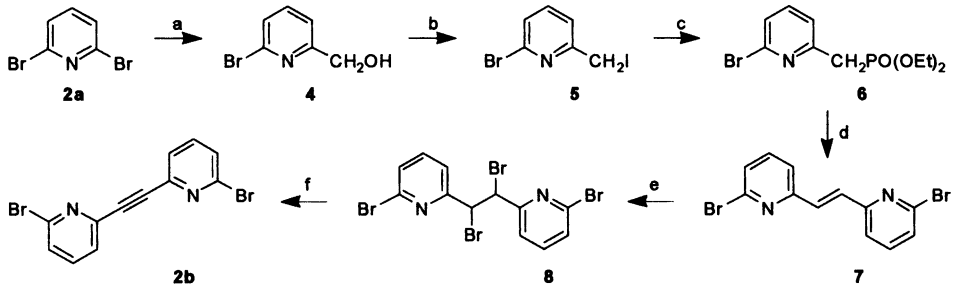


Figure 1.

* Corresponding authors. Fax: +81-6-6879-8474; e-mail: kawano@sanken.osaka-u.ac.jp

0040-4039/02/$ - see front matter
PII: S0040-4039(02)01542-3

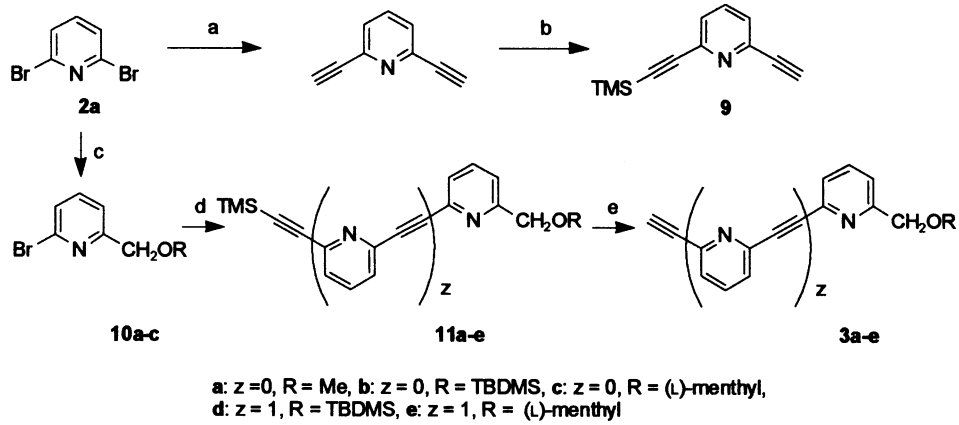


Scheme 1. Preparation of key intermediate **2b**. *Reagents and conditions*: (a) (1) *n*-BuLi, THF, −78°C, (2) DMF, THF, −78°C, (3) $NaBH_4$, THF, 0°C; (b) (1) MsCl, Et_3N, DMAP, THF, −40°C, (2) NaI, acetone, 60°C; (c) $P(OEt)_3$, 150°C; (d) (1) NaH, THF, rt, (2) 2-bromo-6-formylpyridine, THF, rt; (e) Br_2, $CHCl_3$, rt; (f) *tert*-BuOK, THF, rt.

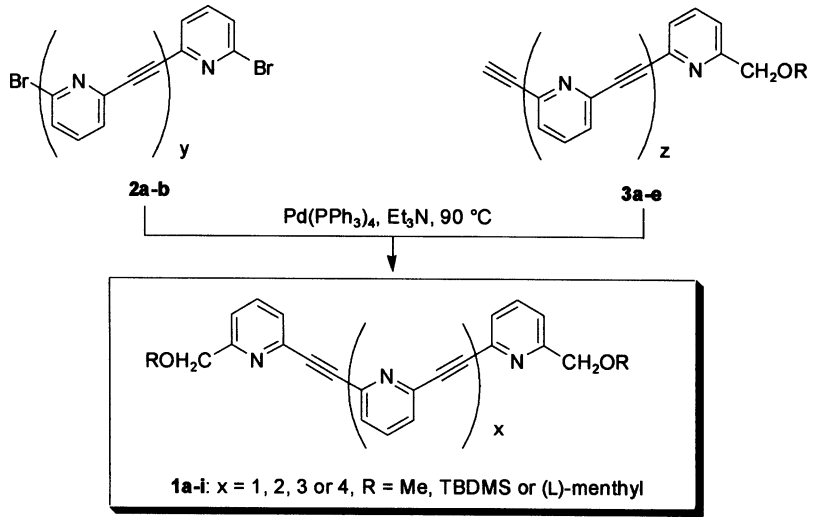
150°C gave the phosphonate **6** in quantitative yield. Subjection of 2-bromo-6-formylpyridine, which was prepared by oxidation of alcohol **4** with 1-iodoxybenzoic acid (IBX)[11] in dimethylsulfoxide (DMSO) at room temperature, to a Horner–Wadsworth–Emmons reaction with the sodium salt of **6** in THF at room temperature afforded exclusively *trans*-disubstituted ethylene derivative **7** in 92% yield. Bromination of **7** with bromine in chloroform at room temperature gave the tetrabromide **8** in 92% yield. Dehydrobromination of **8** with potassium *tert*-butoxide at room temperature yielded the desired product **2b** in 90% yield.

Scheme 2 shows the synthesis of other key intermediates **3a**–**e**. 2,6-Bis(ethynyl)pyridine, which was also prepared from **2a**, was converted into mono TMS–ethynyl substituted pyridine **9** by treatment with ethylmagnesium bromide, followed by mono-silylation with trimethylsilyl chloride (TMSCl) in THF at room temperature in 64% yield. The cross-coupling reaction of bromopyridine derivatives **10a**,[2] **10b**[10] and **10c**[4] with (trimethylsilyl)acetylene (TMSA) or compound **9** in the presence of a catalytic amount of $Pd(PPh_3)_4$ in diethylamine at 60°C gave the corresponding TMS-protected derivatives **11a**–**e** in 83–99% yields. Cleavage of the silyl group with potassium hydroxide (KOH) in methanol at 0°C afforded the desired products **3a**–**e** in 88, 92, 90, 97, and 95% yields, respectively.

The synthesis of oligo(2-ethynylpyridines) **1a**–**i** were achieved by the cross-coupling reaction of **2** with two equivalents of **3** in the presence of a catalytic amount of $Pd(PPh_3)_4$ in diethylamine at 90°C (Scheme 3 and Table 1). Isolated yields of compounds **1** decreased with an increase in the molecular weight of **1**, due to their poor solubility. Especially, compounds **1h** and **1i** were only dissolved in higher polar solvents such as DMSO and DMF. The pure oligo(2-ethynylpyridines) **1a**–**i** were obtained as colorless crystals or white powders, and characterized by spectroscopy (NMR, IR, and FAB mass) and elemental analysis.[12] All data were consistent with the proposed structures. Slight bathochromic shift with elongation of conjugated systems was observed in absorption spectra of **1** (λ_{max} 321 nm for **1b** ($x=1$), 323 nm for **1d** ($x=2$), 325 nm for **1f** ($x=3$), and 327 nm for **1h** ($x=4$)). Furthermore, compounds **1** were found to emit fluorescence around 341–346 nm. As a typical example, excitation of **1a** at 297 nm gave fluorescence around 341 nm. Therefore, the π-conjugated framework of compounds **1** should function as a novel fluorescent probe. Furthermore, treatment of a colorless solution of compound **1h**, as a typical example, in dichloromethane with a colorless solution of copper(I) salts in dichloromethane at room temperature resulted in the formation of a yellow solution of **1h**–copper(I) complex. The resulting yellow solution returned to a colorless solution after addition of acetonitrile, indica-



Scheme 2. Preparation of ethynylpyridines **3a**–**e**. *Reagents and conditions*: (a) (1) TMSA, $PdCl_2(PPh_3)_2$, CuI, Et_2NH, rt, (2) TBAF, THF, rt; (b) (1) EtMgBr, THF, rt, (2) TMSCl, rt; (c) see Refs. 2, 4 and 10; (d) TMSA or compound **9**, $Pd(PPh_3)_4$, Et_2NH, 60°C; (e) KOH, MeOH, 0°C.



Scheme 3.

Table 1. Synthesis of oligo(2-ethynylpyridines) **1a–i**

Entry	Cmpd **2**[a]	Cmpd **3**	R	Product **1**	Yield (%)[b]
1	**2a**	**3a** ($z=0$)	Me	**1a** ($x=1$)	93
2	**2a**	**3b** ($z=0$)	TBDMS	**1b** ($x=1$)	95
3	**2a**	**3c** ($z=0$)	(L)-Menthyl	**1c** ($x=1$)	92
4	**2b**	**3b**	TBDMS	**1d** ($x=2$)	96
5	**2b**	**3c**	(L)-Menthyl	**1e** ($x=2$)	86
6	**2a**	**3d** ($z=1$)	TBDMS	**1f** ($x=3$)	80
7	**2a**	**3e** ($z=1$)	(L)-Menthyl	**1g** ($x=3$)	75
8	**2b**	**3d**	TBDMS	**1h** ($x=4$)	71
9	**2b**	**3e**	(L)-Menthyl	**1i** ($x=4$)	68

[a] Compound **2a** ($y=0$); compound **2b** ($y=1$).
[b] Isolated yield.

tive of the exchange of ligand. This finding indicates that compounds **1** might also function as a copper(I) scavenger.

In conclusion, we have synthesized new oligo(2-ethynylpyridines) **1** from two key intermediates **2** and **3**. Several novel reaction intermediates in this study, such as compounds **7** and **8**, would also function as synthetic blocks for the construction of oligo(pyridines) as well as compounds **2** and **3**, although the synthetic methods reported in this study are conventional ones. Therefore, further modification of the synthetic route by using these synthetic blocks would lead to the generation of a variety of functionalized oligo(2-ethynylpyridines). In addition, our synthetic methods are also of particular importance in that all compounds in this study were derived from only one starting material, 2,6-dibromopyridine. Further studies on the elongation of conjugated systems are now under investigation.

Acknowledgements

We thank the Material Analysis Center of our institute for assisting with elemental analysis.

References

1. For recent reviews, see: (a) Tschierske, C. *Angew. Chem., Int. Ed.* **2000**, *39*, 2454–2458; (b) Ziessel, R. *Synthesis* **1999**, 1839–1865; (c) Constable, E. C. *Pure Appl. Chem.* **1996**, *68*, 253–260; (d) Constable, E. C. *Prog. Inorg. Chem.* **1994**, *42*, 67–138.
2. Kawano, T.; Kuwana, J.; Shinomaru, T.; Du, C.-X.; Ueda, I. *Chem. Lett.* **2001**, 1230–1231.
3. Kawano, T.; Shinomaru, T.; Ueda, I. *Org. Lett.* **2002**, *4*, 2545–2547.
4. Kawano, T.; Kuwana, J.; Du, C.-X.; Ueda, I. *Inorg. Chem.* **2002**, *41*, 4078–4080.
5. For example, see: (a) Baxter, P. N. W. *J. Org. Chem.* **2000**, *65*, 1257–1272; (b) Ziessel, R.; Suffert, J.; Youinou, M.-T. *J. Org. Chem.* **1996**, *61*, 6535–6546 and references cited therein.
6. For example, see: (a) Zaman, M. B.; Tomura, M.; Yamashita, Y. *J. Org. Chem.* **2001**, *66*, 5987–5995; (b) Okubo, J.; Shinozaki, H.; Koitabashi, T.; Yomura, R. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 329–335; (c) Neenan, T. X.; Driessen, W. L.; Haasnoot, J. G.; Reedijk, J. *Inorg. Chim. Acta* **1996**, *247*, 43–49.
7. 2,6-Bis(2-pyridylethynyl)pyridine derivatives, which possess three pyridine rings, are still very rare. See: (a) Inouye, M.; Chiba, J.; Nakazumi, H. *J. Org. Chem.* **1999**,

64, 8170–8176; (b) Inouye, M.; Takahashi, K.; Nakazumi, H. *J. Am. Chem. Soc.* **1999**, *121*, 341–345; (c) Inouye, M.; Miyake, T.; Furusyo, M.; Nakazumi, H. *J. Am. Chem. Soc.* **1995**, *117*, 12416–12425.

8. No synthetic methods for compound **2b** have been reported in the literature to date, although complexation studies by using **2b** have been reported. See: (a) Newkome, G. R.; Onishi, M. *J. Organomet. Chem.* **1980**, *198*, 225–229; (b) Newkome, G. R.; McClure, G. L. *J. Am. Chem. Soc.* **1974**, *96*, 617–618.
9. Cai, D.; Hughes, D. L.; Verhoeven, T. R. *Tetrahedron Lett.* **1996**, *37*, 2537–2540.
10. Tsukube, H.; Uenishi, J.; Higaki, H.; Kikkawa, K.; Tanaka, T.; Wakabayashi, S.; Oae, S. *J. Org. Chem.* **1993**, *58*, 4389–4397.
11. Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019–8022.
12. Selected physical data are as follows. Compound **1d**: white powder, mp 216°C (dec.), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (t, 2H, $J=7.7$ Hz), 7.73 (t, 2H, $J=7.3$ Hz), 7.62 (d, 4H, $J=7.7$ Hz), 7.55 (d, 2H, $J=8.0$ Hz), 7.52 (d, 2H, $J=7.7$ Hz), 4.87 (s, 4H), 0.97 (s, 18H), 0.13 (s, 12H) ppm. IR (KBr) ν 3054, 2930, 2857, 2327, 1577, 1461, 1254, 1112, 852 cm^{-1}. Anal. calcd for $C_{40}H_{46}N_4O_2Si_2$: C, 71.60; H, 6.91; N, 8.35%. Found: C, 71.46; H, 6.72; N, 8.15%. FABMS (NBA) m/z 671 [M+H]$^+$. UV λ_{max} (log ε): 323 (4.65), 302 (4.49), 294 (4.53), 275 (4.47) nm. Fluorescence (ex. 324 nm) 346 nm. Compound **1f**: white powder, mp 258°C (dec.), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76–7.70 (m, 5H), 7.63 (d, 3H, $J=7.8$ Hz), 7.62 (d, 3H, $J=7.8$ Hz), 7.55 (d, 2H, $J=7.8$ Hz), 7.52 (d, 2H, $J=7.6$ Hz), 4.87 (s, 4H), 0.97 (s, 18H), 0.13 (s, 12H) ppm. IR (KBr) ν 3061, 2931, 2857, 2327, 1578, 1455, 1255, 1114, 850 cm^{-1}. Anal. calcd for $C_{47}H_{49}N_5O_2Si_2$: C, 73.11; H, 6.40; N, 9.07%. Found: C, 73.38; H, 6.30; N, 9.18%. FABMS (NBA) m/z 772 [M+H]$^+$. UV λ_{max} (log ε): 325 (4.66), 300 (4.48), 294 (4.51), 285 (4.49) nm. Fluorescence (ex. 325 nm) 344 nm. Compound **1h**: white powder, mp 335°C (dec.), ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77–7.71 (m, 6H), 7.63 (d, 4H, $J=7.6$ Hz), 7.62 (d, 4H, $J=7.6$ Hz), 7.55 (d, 2H, $J=7.8$ Hz), 7.52 (d, 2H, $J=7.8$ Hz), 4.87 (s, 4H), 0.97 (s, 18H), 0.13 (s, 12H) ppm. IR (KBr) ν 3062, 2929, 2856, 2322, 1555, 1454, 1254, 1112, 839 cm^{-1}. Anal. calcd for $C_{54}H_{52}N_6O_2Si_2$: C, 74.28; H, 6.00; N, 9.62%. Found: C, 74.01; H, 5.81; N, 9.53%. FABMS (NBA) m/z 873 [M+H]$^+$. UV λ_{max} (log ε): 327 (4.90), 300 (4.70), 294 (4.71), 290 (4.70) nm. Fluorescence (ex. 326 nm) 344 nm.