Supporting information

Nucleophilic substitution reaction of pyrimidin-2-yl phosphates using amines and thiols as nucleophiles mediated by PEG-400 as an environmentally friendly solvent

Ting Xing, Kai-jie Wei, Zheng-Jun Quan, Xi-Cun Wang

Key Laboratory of Eco-Environment-Related Polymer Materials, Ministry of Education, China, Gansu 730070, P. R. China
Key Laboratory of Polymer Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Gansu 730070, P. R. China
Tel/Fax: +86-931-7971680; E-mail: wangxicun@nwnu.edu.cn.

Table of Contents

The data for Compounds 6.................................................................S2
NMR Spectra for New Compounds in Table 1.............................................S8
NMR Spectra for Compound 5.............................................................S34
NMR Spectra for Compound 6.............................................................S37
General procedure for the synthesis of 6a-6c.
Firstly, a mixture of compound 3k (0.4 mmol) and amid es (4i, 4j, 4k) (0.6 mmol) was added into the reaction tube. Then, CuSO$_4$·5H$_2$O (15 mol%, 0.015g), NaAsc (30 mol%, 0.024g) and BuONa (0.8 mmol, 0.077g) were added into the reaction system in DMSO (3 mL). After the mixture was stirred at 100 °C for 7h (TLC monitoring), the reaction mixture was extracted with water and ethyl acetate. Then, the organic layers were dried over Na$_2$SO$_4$. The crude product was purified by flash chromatography to give pure products 6.

**Methyl 2-benzamido-4-methyl-6-phenylpyrimidine-5-carboxylate (6a)**
Eluent: petroleum ether-EtOAc (4:1) to EtOAc; yield: 97 mg (70%); colourless oil.
IR (KBr): 3440 (s), 2924 (m), 1638 (s), 1560 (w), 1542 (w), 1508 (w), 1458 (w), 1092 (w), 582 (w) cm$^{-1}$.
$^1$H NMR (600 MHz, CDCl$_3$): δ = 7.82-7.81 (m, 3H, ArH), 7.60-7.59 (m, 1H, ArH), 7.54-7.52 (m, 2H, ArH), 7.47-7.44 (m, 4H, ArH), 5.34 (s, 1H, NH), 2.01 (s, 3H, CH$_3$), 0.88 (s, 3H, OCH$_3$).
$^{13}$C NMR (150 MHz, CDCl$_3$): δ = 169.20, 163.99, 162.04, 158.81, 151.34, 146.36, 132.02, 129.89, 129.85, 128.61 (2C), 127.31 (2C), 111.06, 53.88, 22.66.
HRMS (EI): m/z [M + H]$^+$ calcd for C$_{20}$H$_{19}$N$_3$O$_3$: 348.1343; found: 348.1350.

**Methyl 4-methyl-2-(4-methylphenylsulfonamido)-6-phenylpyrimidine-5-carboxylate (6b)**
Eluent: petroleum ether-EtOAc (4:1) to EtOAc; yield: 103 mg (65%); yellow oil.
IR (KBr): 3420 (s), 2960 (m), 1654 (m), 1458 (m), 1260 (w), 1036 (s), 796 (w), 564 (w) cm$^{-1}$.
$^1$H NMR (600 MHz, CDCl$_3$): δ = 7.81-7.79 (m, 1H, ArH), 7.59 (d, J = 5.2 Hz, 2H, ArH), 7.50-7.42 (m, 5H, ArH), 7.30 (d, J = 5.2 Hz, 1H, ArH), 4.95 (s, 1H, NH), 3.58 (s, 3H, Ar-CH$_3$), 2.98 (s, 3H, CH$_3$), 2.59 (s, 3H, OCH$_3$).
$^{13}$C NMR (150 MHz, CDCl$_3$): δ = 166.60, 158.04, 143.51, 139.14, 131.02, 129.66 (2C), 128.45 (2C), 128.17, 127.94 (2C), 127.76, 126.42 (2C), 126.25, 111.12, 52.29, 22.66, 21.49.
HRMS (EI): m/z [M + H]$^+$ calcd for C$_{20}$H$_{21}$N$_3$O$_4$: 398.1169; found: 398.1175.

**Methyl 2-((ethoxycarbonyl)amino)-4-methyl-6-phenylpyrimidine-5-carboxylate (6c)**
Eluent: petroleum ether-EtOAc (4:1) to EtOAc; yield: 86 mg (68%); colourless oil.
IR (KBr): 3425 (s), 2960 (m), 1654 (m), 1458 (m), 1400 (w), 1036 (s), 796 (w), 564 (w) cm$^{-1}$.
$^1$H NMR (600 MHz, CDCl$_3$): δ = 7.60-7.56 (m, 1H, ArH), 7.51-7.49 (m, 2H, ArH), 7.45-7.41 (m, 2H, ArH), 5.34 (s, 1H, NH), 3.82 (q, J = 4.8 Hz, 2H, CH$_2$), 3.54 (s, 3H, OCH$_3$), 2.48 (s, 3H, Ar-CH$_3$), 1.17 (t, J = 4.8 Hz, 3H, CH$_2$CH$_3$).
$^{13}$C NMR (150 MHz, CDCl$_3$): δ = 168.32, 166.08, 162.04, 156.81, 156.12, 151.02 (2C), 146.67 (2C), 128.79, 121.23, 109.98, 54.31, 29.29, 27.19, 14.08.
HRMS (EI): m/z [M + H]$^+$ calcd for C$_{16}$H$_{19}$N$_3$O$_4$: 316.1292; found: 316.1295.
Figure S1. $^1$H NMR of 3g (400 MHz, CDCl$_3$), $^{13}$C NMR of 3g (150 MHz, CDCl$_3$) and $^{31}$P NMR of 3g (400 MHz, CDCl$_3$).
Figure S2. $^1$H NMR of 3h (600 MHz, CDCl$_3$), $^{13}$C NMR of 3h (100 MHz, CDCl$_3$) and $^{31}$P NMR of 3h (600 MHz, CDCl$_3$).
Figure S3. $^1$H NMR of 3i (600 MHz, CDCl$_3$), $^{13}$C NMR of 3i (150 MHz, CDCl$_3$) and $^{31}$P NMR of 3i (600 MHz, CDCl$_3$).
Figure S4. $^1$H NMR of 3j (600 MHz, CDCl$_3$), $^{13}$C NMR of 3j (150 MHz, CDCl$_3$) and $^{31}$P NMR of 3j (600 MHz, CDCl$_3$).
Figure S5. $^1$H NMR of 5a (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5a (100 MHz, CDCl$_3$).
Figure S6. $^1$H NMR of 5b (400 MHz, CDCl3) and $^{13}$C NMR of 5b (150 MHz, CDCl3).
Figure S7. $^1$H NMR of 5c (400 MHz, CDCl₃) and $^{13}$C NMR of 5c (100 MHz, CDCl₃).
Figure S8. $^1$H NMR of 5d (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5d (100 MHz, CDCl$_3$).
Figure S9. $^1$H NMR of 5e (400 MHz, CDCl₃) and $^{13}$C NMR of 5e (100 MHz, CDCl₃).
Figure S10. $^1$H NMR of 5f (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5f (100 MHz, CDCl$_3$).
Figure S11. $^1$H NMR of 5g (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5g (100 MHz, CDCl$_3$).
Figure S12. $^1$H NMR of 5h (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5h (150 MHz, CDCl$_3$).
Figure S13. $^1$H NMR of 5i (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5i (100 MHz, CDCl$_3$).
Figure S14. \( ^1H \) NMR of Sj (400 MHz, CDCl$_3$) and \( ^{13}C \) NMR of Sj (100 MHz, CDCl$_3$).
Figure S15. $^1$H NMR of 5k (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5k (100 MHz, CDCl$_3$).
Figure S16. $^1$H NMR of SI (400 MHz, CDCl₃) and $^{13}$C NMR of SI (100 MHz, CDCl₃).
Figure S17. $^1$H NMR of 5m (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5m (100 MHz, CDCl$_3$).
Figure S18. $^1$H NMR of 5n (400 MHz, CDCl₃) and $^{13}$C NMR of 5n (100 MHz, CDCl₃).
Figure S19. $^1$H NMR of 5o (600 MHz, CDCl$_3$) and $^{13}$C NMR of 5o (150 MHz, CDCl$_3$).
Figure S20. $^1$H NMR of 5p (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5q (150 MHz, CDCl$_3$).
Figure S21. $^1$H NMR of 5q (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5q (100 MHz, CDCl$_3$).
Figure S22. $^1$H NMR of 5r (600 MHz, CDCl3) and $^{13}$C NMR of 5r (150 MHz, CDCl3).
Figure S23. $^1$H NMR of 5s (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5s (100 MHz, CDCl$_3$).
Figure S24. $^1$H NMR of 5t (600 MHz, CDCl$_3$) and $^{13}$C NMR of 5t (150 MHz, CDCl$_3$).
Figure S25. $^1$H NMR of 5u (600 MHz, CDCl$_3$) and $^{13}$C NMR of 5u (150 MHz, CDCl$_3$).
Figure S26. $^1$H NMR of 5v (400 MHz, CDCl$_3$) and $^{13}$C NMR of 5v (100 MHz, CDCl$_3$).
Figure S27. $^1$H NMR of 5w (400 MHz, CDCl3) and $^{13}$C NMR of 5w (100 MHz, CDCl3).
Figure S28. $^1$H NMR of 5x (600 MHz, CDCl$_3$) and $^{13}$C NMR of 5x (150 MHz, CDCl$_3$).
Figure S29. $^1$H NMR of 5y (400 MHz, CDCl3) and $^{13}$C NMR of 5y (100 MHz, CDCl3).
Figure S30. $^1$H NMR of 5z (600 MHz, CDCl$_3$) and $^{13}$C NMR of 5z (100 MHz, CDCl$_3$).
Figure S31. $^1$H NMR of 6a (600 MHz, CDCl$_3$) and $^{13}$C NMR of 6a (150 MHz, CDCl$_3$).
Figure S32. $^1$H NMR of 6b (600 MHz, CDCl$_3$) and $^{13}$C NMR of 6b (100 MHz, CDCl$_3$).
Figure S33. $^1$H NMR of 6c (600 MHz, CDCl$_3$) and $^{13}$C NMR of 6c (150 MHz, CDCl$_3$).