Pergamon

Tetrahedron Letters 40 (1999) 6373–6376

TETRAHEDRON
LETTERS

Palladium-catalysed coupling of vinyl phosphates with aryl or heteroaryl boronic acids. Application to the synthesis of substituted nitrogen containing heterocycles

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Received 25 March 1999; accepted 18 June 1999

Abstract

Unusual substituted nitrogen-containing heterocycles were prepared in three steps from commercially available derivatives via an extension of the Suzuki reaction involving the palladium-catalysed coupling of vinyl phosphate with aryl or heteroarylboronic acids. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords: coupling reactions; palladium; palladium compounds; boronic acids; benzoxazines; benzothiazines.

The palladium-catalysed cross-coupling of organoboron compounds with organic halides or triflates, known as the Suzuki reaction, has attracted increasing attention over the last few years. Originally reported in 1981 for the palladium-catalysed cross-coupling of arylboronic acids with aryl halides in the presence of a base,[1] this reaction has seen its scope extended to the coupling of aryl boronic acids with heteroaryl halides,[2] aryl or vinyl triflates,[3] vinyl bromides,[4] and allyl bromides.[5] Recent developments in this versatile reaction also include the coupling of heteroaromatic boronic acids,[6] palladium-mediated C–C and C–S bond formation on solid support.[7]

Due to their excellent leaving group properties, aryl and vinyl trifluoromethane sulfonates (triflates), have seen their applications broaden considerably since their introduction by Stang 30 years ago.[8] They constitute versatile intermediates which are easily prepared from the corresponding carbonyl compounds or enolates by treatment with triflic anhydride,[9] *N*-pyridyltriflimides,[10] or *N*,*N*-bis(trifluoromethanesulfonyl)aniline.[11] These reagents are certainly easily available but constitute nevertheless quite expensive derivatives. Moreover, vinyl triflates sometimes exhibit a lack of stability. It was previously shown by Nicolaou[12] that cyclic ketene acetal phosphates could constitute an attractive alternative to their triflate counterparts thanks to their lower cost, higher stability and efficiency in formation and in coupling reactions.

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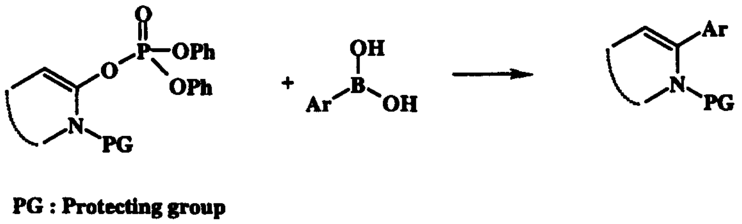
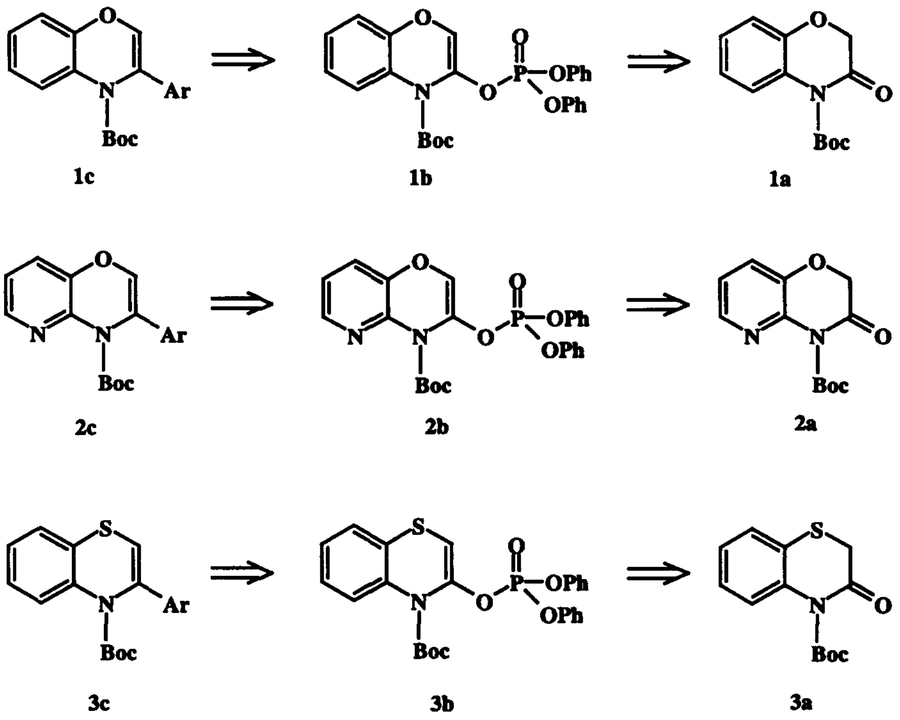
PII: S0040-4039(99)01160-0

To the best of our knowledge the palladium-catalysed coupling reactions of boronic acids and vinyl phosphates have never been reported so far. In this letter we describe the synthesis of unusual substituted nitrogen-containing heterocycles via an extension of the Suzuki reaction (Scheme 1).



Scheme 1.

The procedure was tested in the 4*H*-benzo[1,4]oxazine, 4*H*-pyrido[3,2-*b*][1,4]oxazine and 4*H*-benzo[1,4]thiazine series as shown in Scheme 2.



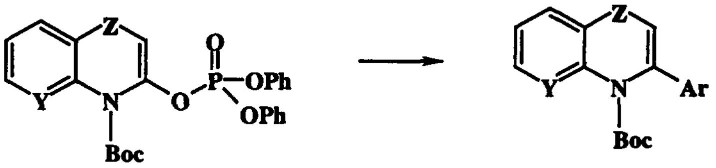
Scheme 2.

N-Boc lactams **1a**, **2a** and **3a** were prepared in nearly quantitative yields (96, 98 and 91%, respectively), from the corresponding commercially available N–H lactams by treatment with di-*tert*-butyl dicarbonate in tetrahydrofuran, at room temperature in the presence of DMAP.

Vinyl phosphates **1b**, **2b** and **3b** were easily obtained from the corresponding *N*-Boc lactams by trapping their lithium enolates (LDA 1.2 equiv., TMEDA 1.2 equiv., THF, –78°C) with diphenylchlorophosphate (1.2 equiv.) as shown in Scheme 3.[13]

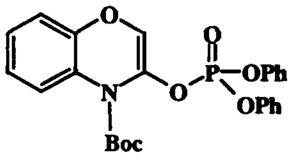
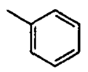
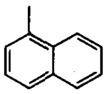
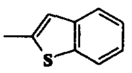
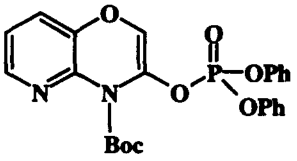
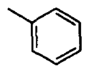
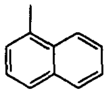
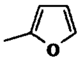
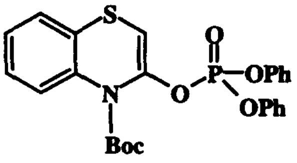
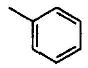
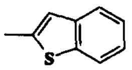
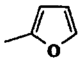
Palladium-catalysed coupling was then performed by adapting a procedure previously described by Snieckus.[14] A typical procedure is as follows: to a suspension of $Pd(PPh_3)_4$ (0.05 equiv.) in anhydrous DME vinyl phosphate was added (1 equiv.) and the mixture was stirred for 10 min at room temperature.

Table 1
Synthesis of 3-substituted-4*H*-benzo[1,4]oxazines **1c**, 3-substituted-4*H*-pyrido[3,2-*b*][1,4]oxazines **2c** and 3-substituted-4*H*-benzo[1,4]thiazines **3c**[15]



1b Y=C, Z=O
2b Y=N, Z=O
3b Y=C, Z=S

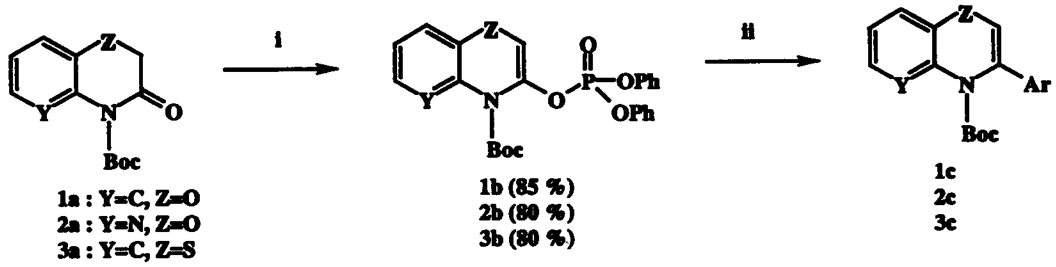
1c
2c
3c

Vinylphosphate	Ar	Yield[a] %
		75
		74
		70
		78
		98
		85
		78
		71
		92

a : isolated yield

Boronic acid (1.5 equiv.) in a minimum of ethanol and aqueous Na_2CO_3 (2 M solution, 2.0 equiv.) were then added and the mixture was refluxed for 0.5 h.

Table 1 summarises the results of the palladium-catalysed coupling reactions between vinyl phosphates **1b**, **2b** and **3b** and some typical aryl or heterocyclic boronic acids.



Scheme 3. (i) LDA 1.2 equiv., TMEDA 1.2 equiv., THF, −78°C, $ClPO(OPh)_2$ 1.2 equiv.; (ii) $Pd(PPh_3)_4$ 0.05 equiv., DME, rt then $ArB(OH)_2$ 1.5 equiv., Na_2CO_3 2 equiv., EtOH, reflux

To sum up we have developed a new versatile and efficient method for the preparation of little known nitrogen-containing heterocycles.

Further investigations are now in progress for an extension of this Suzuki type procedure.

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13. 4-(*tert*-Butoxycarbonyl)-3-[(diphenoxyphosphoryl)oxo]-4*H*-benzo[1,4]oxazine (**1b**), m.p.: 64–65°C. IR (KBr): ν cm^{-1} 1732 (C=O), 1591 and 1489 (C=C), 1315 (P=O). ^1H NMR ($CDCl_3$, 250 MHz): δ ppm 1.46 (s, 9H, $(CH_3)_3C$); 6.70 (d, 1H, H_2, $J_{2,P}$=4 Hz); 6.91 to 7.41 (m, 14H, H_{arom}). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ ppm 27.9 ($3CH_3$, $(CH_3)_3C$); 83.2 (C, $C(CH_3)_3$); 115.9 (CH); 119.9 (4CH); 123.5 (CH); 124.9 (CH); 125.6 (2CH); 126.6 (CH); 128.3 (CH); 128.5 (C); 129.8 (4CH); 132.3 (C); 150.2 (2C); 150.9 (C); 151.7 (C). SM (IS): *m/z*=482 (M+1). 4-(*tert*-Butoxycarbonyl)-3-[(diphenoxyphosphoryl)oxo]-4*H*-pyrido[3,2-*b*][1,4]oxazine (**2b**), m.p.: 94°C. IR (KBr): ν cm^{-1} 1713 (C=O), 1590 and 1487 (C=C), 1313 (P=O). ^1H NMR ($CDCl_3$, 250 MHz): δ ppm 1.46 (s, 9H, $(CH_3)_3C$); 6.75 (d, 1H, H_2, $J_{2,P}$=3.5 Hz); 7.12 (dd, 1H, H_7, $J_{6,7}$=5 Hz, $J_{7,8}$=8 Hz); 7.19 to 7.37 (m, 11H, 10H_{arom} and H_8); 8.29 (dd, 1H, H_6, $J_{6,7}$=5 Hz, $J_{6,8}$=1.5 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ ppm 28.2 ($3CH_3$, $(CH_3)_3C$); 84.1 (C, $(CH_3)_3C$); 120.3 (4CH); 122.7 (CH, C_7); 124.4 (CH); 126.0 (CH); 128.1 (CH); 128.2 (CH, C_2); 130.2 (4CH); 133.0 (C); 141.7 (C); 144.1 (CH, C_6); 147.0 (C); 150.5 (2C); 151.5 (C). SM (IS): *m/z*=483 (M+1). 4-(*tert*-Butoxycarbonyl)-3-[(diphenoxyphosphoryl)oxo]-4*H*-benzo[1,4]thiazine (**3b**), oil. IR (film): ν cm^{-1} 1730 (C=O), 1590 and 1489 (C=C), 1334 (P=O). ^1H NMR ($CDCl_3$, 250 MHz): δ ppm 1.45 (s, 9H, $(CH_3)_3C$); 6.20 (d, 1H, H_2, $J_{2,P}$=3 Hz); 7.13 to 7.32 (m, 14H, H_{arom}). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ ppm 28.1 ($3CH_3$, $(CH_3)_3C$); 83.4 (C, $(CH_3)_3C$); 103.3 (CH); 120.1 (4CH); 120.2 (CH); 125.9 (CH); 126.6 (CH); 126.7 (CH); 127.0 (CH); 127.2 (CH); 130.0 (4CH); 132.6 (C); 137.4 (C); 137.8 (C); 150.4 (2C); 151.5 (C). SM (IS): *m/z*=498 (M+1).
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15. Compounds **1c**, **2c** and **3c** have been satisfactorily characterised.