A key intermediate for the synthesis of this compound was the functionalized 1,3-diarylallene 1, which was prepared by a copper-promoted SN2-substitution reaction of the corresponding propargylic acetate (Figure 1).1,2

![Figure 1](image)

For a fine-tuning of the complexation properties, allenophanes containing heterocyclic rings (e.g., pyridines) are particularly interesting. Towards this end, allenes of type 2 containing one or two functionalized pyridine rings (as well as the corresponding molecules with the heteroatom in the 3- or 4-position with respect to the allenic moiety) were required as building blocks. Interestingly, only a limited number of allenyl-substituted pyridines has been reported in the literature so far.3–5 and none of these has been prepared by a metal-mediated SN2-substitution of a propargylic precursor. Therefore, we first examined the synthesis of unfunctionalized pyridylallenes with the intention to subsequently apply the most suitable reaction conditions to the corresponding functionalized target molecules.

It was quickly established that the position of the pyridine nitrogen atom with respect to the propargylic acetate strongly influences the outcome of the substitution reaction. Whereas the reaction of substrate 3a with an excess of the magnesium cuprate MeMgCl·CuI·LiBr1,2 provided the desired 2-allenyl-substituted pyridine 4 with 46% yield, the analogous treatment of the regioisomeric substrate 3b gave the same product with only 17% yield (Scheme 1). In both cases, rather low substrate concentrations in the range of 9–12 mmol/L had to be used; with higher concentrations, only polymeric products were obtained. In contrast to this, both substrates 5a and 5b bearing the nitrogen atom in 3-position with respect to the propargylic bridge could be converted into pyridylallene 6 without difficulty (82% and 89% yield, respectively).

![Scheme 1](image)
parts 5 could be converted without difficulty into the desired allenes 7 and 8 by treatment with an excess of phenylzinc chloride and 5 mol% of Pd(PPh₃)₄ (Scheme 2). Under these conditions, however, allenes 7a/b were obtained with slightly higher yields (78/82%) than the isomers 8a/b (69/46%), indicating that the reaction is not affected by a possible chelate formation between substrate and organometallic reagent.

Scheme 2

The application of these reaction conditions to propargylic acetates bearing functionalized pyridine rings confirms the observations made with the unfunctionalized substrates 3 and 5. Thus, treatment of substrates 9 and 11, respectively, with MeMgCl·CuI·LiBr furnished the functionalized pyridylallenes 10 and 12 with 79% and 89% yield, whereas the corresponding reactions with propargylic acetates 13 and 14 failed (Scheme 3). In the latter cases, chelation of the cuprate between the pyridine nitrogen and the acetyl or acetal oxygen atoms may be responsible for the outcome.

As expected, the palladium-catalyzed S₂N₂-substitution reaction with phenylzinc chloride proceeded smoothly even with functionalized propargylic acetates which are capable of forming chelate complexes (a collection of pyridylallenes prepared by this route is given in Figure 2). The reactions were carried out with 5 mol% of Pd(PPh₃)₄ in THF and gave the products 15–18 with yields ranging from 71–94%, i.e., even an allene with two pyridine rings (15) is accessible with this method.

In summary, the S₂N₂-substitution reaction of various functionalized and unfunctionalized pyridyl-substituted propargylic acetates with the magnesium cuprate MeMgCl·CuI·LiBr was found to proceed efficiently only with substrates which cannot form a chelate complex with the cuprate. In contrast to this, the palladium-catalyzed substitution with phenylzinc chloride gave the desired pyridylallenes with good to excellent yields in all cases examined, i.e., the reaction is not influenced by the position of the pyridine nitrogen atom and the possibility of chelate complex formation. With the richly functionalized pyridylallenes 10, 12, and 15–18 in hand, we now pursue their use in the synthesis of allenic pyridinophanes.

Scheme 3
Melting points were determined with a Büchi 510 capillary mp apparatus and are uncorrected. IR spectra were obtained with a Bruker IFS 66 spectrometer either in KBr pellets or as liquid film between NaCl plates. 1H and 13C NMR spectra were recorded in benzene-d6 or DMSO-d6 with a Bruker DRX 400 or a Bruker DRX 500 spectrometer using the signals of the undeuterated solvent as the standard. EI mass spectra were measured with a Finnigan MAT 8230 or a JEOL JMS-SX102A mass spectrometer, ESI spectra with a Finnigan TSQ 7000 mass spectrometer. Elemental analyses were performed on a LECO elemental analyser CHNS-932.

All reactions were carried out under an argon atmosphere in dried glassware. THF was distilled from sodium/benzophenone prior to use. Lithium bromide was dried in vacuo at 120 °C and stored under an argon atmosphere. Zinc chloride was dried by heating with freshly distilled thionyl chloride and was used as a 2 M solution in THF after removal of the thionyl chloride in vacuo. The substrates 3 and 5 were obtained by addition of the corresponding titanium acetylide to the appropriate ketone 9 and subsequent acylation with acetyl chloride–Et3N–DMAP. The functionalized propargylic acetates were prepared accordingly with 2-acetyl-6-bromopyridine, 3-acetyl-6-bromopyridine, and 6-bromo-2-formylpyridine as the starting materials. The products were purified by column chromatography or radial chromatography using a Harrison Research 8924 Chromatotron.

Copper-Mediated S2,2-Substitution of Propargylic Acetates; General Procedure

To a solution of CuI (4.0 equiv) and LiBr (4.0 equiv) in THF was added at −5 °C MeMgCl (4.0 equiv) in THF. After stirring for 15 min at −5 °C, the cuprate solution was cooled to −40 °C, and the cuprate solution was cooled to −5 °C. The mixture was warmed to r.t. within 16 h. After addition of sat. aq NH4Cl, the layers were separated and the aq layer was washed with Et2O. The substrates 3 and 5 were obtained by addition of the appropriate titanium acetylides to the appropriate ketone 9 and subsequent acylation with acetyl chloride–Et3N–DMAP. The functionalized propargylic acetates were prepared accordingly with 2-acetyl-6-bromopyridine, 3-acetyl-6-bromopyridine, and 6-bromo-2-formylpyridine as the starting materials. The products were purified by column chromatography or radial chromatography using a Harrison Research 8924 Chromatotron.

Palladium-Catalyzed S2,2-Substitution of Propargylic Acetates; General Procedure

To a solution of ZnCl2 (3.0 equiv) in THF was added PhMgCl in THF, and the mixture was stirred for 30 min at r.t. After cooling to −50 °C, Pd(PPh3)4 in THF and the propargylic acetate (1.0 equiv) in THF were added subsequently, and the mixture was warmed up to r.t. within 6 h. After addition of a sat. aq NH4Cl, the layers were separated and the aq layer was washed with Et2O. The combined organic phases were dried (Na2SO4), the solvent was removed under reduced pressure, and the crude product was purified by chromatography.

Palladium-Catalyzed S2,2-Substitution of Propargylic Acetates; General Procedure

To a solution of ZnCl2 (3.0 equiv) in THF was added PhMgCl in THF, and the mixture was stirred for 30 min at r.t. After cooling to −50 °C, Pd(PPh3)4 in THF and the propargylic acetate (1.0 equiv) in THF were added subsequently, and the mixture was warmed up to r.t. within 6 h. After addition of a sat. aq NH4Cl, the layers were separated and the aq layer was washed with Et2O. The combined organic phases were dried (Na2SO4), the solvent was removed under reduced pressure, and the crude product was purified by chromatography.

2-(1-Methyl-3-phenylbuta-1,2-dienyl)pyridine (4)
The compound was obtained from CuI (143 mg, 0.75 mmol) and LiBr (65 mg, 0.75 mmol) in THF (17 mL), MeMgCl (3.0 M solution in THF: 0.25 mL, 0.75 mmol), and 2a (50 mg, 0.19 mmol) in THF (5 mL). Purification of the crude product by radial chromatography (SiO2; pentane–Et2O, 1:1) furnished 4.

Yield: 19 mg (46%); reddish oil.

Alternatively, 4 was prepared from CuI (286 mg, 1.5 mmol) and LiBr (130 mg, 1.5 mmol) in THF (25 mL), MeMgCl (3.0 M solution in THF: 0.5 mL, 1.5 mmol), and 2b (100 mg, 0.38 mmol) in THF (5 mL). Purification of the crude product by radial chromatography (SiO2; pentane–Et2O, 1:1) furnished 4.

Yield: 14 mg (17%); brown oil.

IR (neat): 1938 (w, C=C=C) cm−1.

MS (EI, 70 eV): m/z (%): 221 (93, M+), 220 (100, M+–H), 206 (30).

HRMS (EI): calcd for C16H12N (221.30): 221.1204; found: 221.1204.

2-(1-Methyl-3-phenylbuta-1,2-dienyl)pyridine (6)
The compound was obtained from CuI (143 mg, 0.75 mmol) and LiBr (65 mg, 0.75 mmol) in THF (15 mL), MeMgCl (3.0 M solution in THF: 0.25 mL, 0.75 mmol), and 5a (47 mg, 0.18 mmol) in THF (5 mL). Purification of the crude product by column chromatography (SiO2; pentane–Et2O, 1:1) furnished 6.

Yield: 32 mg (82%); yellow oil.

Alternatively, 6 was prepared from CuI (1.44 g, 7.6 mmol) and LiBr (0.66 g, 7.6 mmol) in THF (65 mL), MeMgCl (3.0 M solution in THF: 2.5 mL, 7.5 mmol), and 5b (500 mg, 1.9 mmol) in THF (10 mL). Purification of the crude product by column chromatography (SiO2; pentane–Et2O, 1:1) furnished 6.

Yield: 373 mg (89%); yellow oil.

IR (neat): 1936 (w, C=C=C) cm−1.

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 0.45 mL, 0.9 mmol), PhMgCl (2.0 M solution in THF; 0.45 mL, 0.9 mmol), Pd(PPh₃)₄ (11 mg, 0.01 mmol) in THF (0.5 mL), and 3a (47 mg, 0.18 mmol) in THF (2 mL). Purification of the crude product by column chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 7a.

Yield: 39 mg (78%); yellow crystals; mp 79 °C.

IR (KBr): 3930 (w, C=C) cm⁻¹.

¹H NMR (DMSO-d₆): δ = 8.57 (dd, 1 H, J = 4.8, 1.8, 0.8 Hz, 6-H), 7.80 (dt, 1 H, J = 7.8, 1.8 Hz, 4-H), 7.50–7.25 (m, 12 H, H arom ), 2.27 (s, 3 H, CH₃).

¹³C NMR (DMSO-d₆): δ = 120.3 (C-2'), 156.6 (C-2), 149.7 (+, C-6), 136.6, 136.4 (C-1', C-1''), 136.1 (+, C-4'), 129.3, 128.9, 128.6 (3 +, 6 C arom ), 126.7, 126.7, 126.5 (2 +, C-3, C-5), 126.3 (+, 2 C arom ), 123.0, 121.7 (+, C-4, C-4'), 113.1 (C-1'), 105.1 (C-3'), 16.7 (s, CH₃).

MS (EI): m/z (%) = 283 (M⁺, 100).

HRMS (EI): caled for C₁₂H₁₂N (283.37): 283.1361; found: 283.1359.

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 0.55 mL, 1.1 mmol), PhMgCl (2.0 M solution in THF; 0.55 mL, 1.1 mmol), Pd(PPh₃)₄ (22 mg, 0.02 mmol) in THF (1 mL), and 3b (100 mg, 0.38 mmol) in THF (2 mL). Purification of the crude product by column chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 7b.

Yield: 39 mg (82%); yellow crystals; mp 94 °C.

IR (KBr): 1924 (w, C=C) cm⁻¹.

¹H NMR (DMSO-d₆): δ = 8.59 (m, 1 H, 6-H), 7.75 (d, 1 H, J = 7.9, 1.7 Hz, 4-H), 7.58 (d, 1 H, J = 7.9 Hz, H arom ), 7.42–7.38 (m, 4 H, H arom ), 7.35–7.31 (m, 6 H, H arom ), 7.25 (m, 1 H, H arom ), 2.28 (s, 3 H, CH₃).

¹³C NMR (DMSO-d₆): δ = 209.7 (C-2'), 155.9 (+, C-6), 149.6 (+, C-2, C-4), 137.0 (C-1', C-1''), 135.9 (+, C-3), 128.9, 128.8, 127.8, 121.9, 121.5 (5 +, C arom ), 113.1 (x, C-3'), 106.5 (C-1'), 16.2 (+, CH₃).

MS (EI): m/z (%) = 283 (92, M⁺, 100). Anal. caled for C₁₂H₁₂N: 283.37; C, 89.01; H, 6.05; N, 4.94. Found: C, 89.10; H, 6.10; N, 4.70.

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 0.17 mL, 0.34 mmol), PhMgCl (2.0 M solution in THF; 0.17 mL, 0.34 mmol), Pd(PPh₃)₄ (8 mg, 0.007 mmol) in THF (0.5 mL), and 5a (30 mg, 0.11 mmol) in THF (2 mL). Purification of the crude product by radial chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 8a.

Yield: 22 mg (69%); colorless oil.

IR (neat): 1932 (w, C=C) cm⁻¹.

³⁻¹H NMR (CD₃OD): δ = 9.12 (br s, 1 H, 2-H), 8.56 (d, 1 H, J = 4.0 Hz, 6-H), 7.53–7.44 (m, 5 H, H arom ), 7.21–7.09 (m, 6 H, H arom ), 6.78 (dd, 1 H, J = 7.9, 4.8, 0.7 Hz, H arom ), 2.04 (s, 3 H, CH₃).

¹³C NMR (CD₃OD): δ = 208.0 (C-2'), 150.3, 149.0 (2 +, C-2, C-6), 136.4, 136.2 (C-1', C-1''), 135.2 (+, C-4'), 129.0, 128.9, 128.5 (3 +, 6 C arom ), 127.9, 127.6 (2 +, C-4', C-4''), 126.2 (+, 2 C arom ), 109.5 (C-5'), 105.0 (C-3'), 16.7 (+, CH₃).

MS (EI): M/z (%) = 283 (100, M⁺).

HRMS (EI): caled for C₁₂H₁₂N (283.37): 283.1361; found: 283.1362.

3-(1-Methyl-3,3-diphenylpropa-1,2-dienyl)pyridine (8b)

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 1.0 mL, 2.0 mmol), PhMgCl (2.0 M solution in THF; 1.0 mL, 2.0 mmol), Pd(PPh₃)₄ (22 mg, 0.02 mmol) in THF (1 mL), and 5b (100 mg, 0.38 mmol) in THF (2 mL). Purification of the crude product by column chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 8b.

Yield: 49 mg (46%); colorless crystals; mp 96 °C.

IR (KBr): 2264 (w, C=C) cm⁻¹.

¹H NMR (DMSO-d₆): δ = 8.68 (d, 1 H, J = 2.4 Hz, 2-H), 8.46 (dd, 1 H, J = 4.7, 1.6 Hz, 6-H), 7.83 (d, 1 H, J = 8.0 Hz, 4-H), 7.42–7.38 (m, 5 H, H arom ), 7.34–7.31 (m, 6 H, H arom ), 2.28 (s, 3 H, CH₃).

¹³C NMR (DMSO-d₆): δ = 207.4 (C-2'), 148.7, 147.8 (2 +, C-2, C-6), 132.6 (C-1', C-1''), 132.6 (+, C-4), 132.3 (C-3), 128.9, 128.8 (2 +, C arom ), 123.3 (+, C-5), 113.0 (C-3'), 101.8 (C-1'), 16.4 (+, CH₃).

MS (EI): m/z (%) = 283 (60, M⁺, 282 (100, M⁺–H).

HRMS (EI): caled for C₁₂H₁₀N (282.1383); found: 282.1283.
Yield: 80 mg (89%); orange oil.

IR (neat): v 3600–2700 cm⁻¹, 1738, 1644, 1471, 1385, 1272, 1185, 1120, 1066, 679 cm⁻¹.

HRMS (EI) calcd for C₂₉H₃₀N₂O₂Si (466.66): 466.2065; found: 466.2066.

MS (EI, 70 eV): m/z (%) = 465 (100, M⁺).

HRMS (EI) calcd for C₅H₈O₃Si (465.66): 465.2124; found: 465.2123.

PAPER

2-(1,3-Dioxan-2-yl)-6-[1-phenyl-3-(3-trimethylsilylthiethyl)-2-pyrindinyl]buta-1,2-dienylpyridine (17)

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 0.2 mL, 0.4 mmol), PhMgCl (2.0 M solution in THF; 0.2 mL, 0.4 mmol), Pd(PPh₃)₄ (9 mg, 0.008 mmol) in THF (0.5 mL), and 2-[1-acetoxy-3-[4-(1,3-dioxan-2-yl)phenyl]-1-methylprop-2-ynyl]-6-(trimethylsilyl)pyridine (68 mg, 0.15 mmol) in THF (2 mL).

Purification of the crude product by column chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 17.

Yield: 60 mg (85%); slightly yellow oil.

IR (neat): 2160 (w, C=C), 1391 (s, C-O), 1367 (s, C-H), 1295 (s, C-Si), 1214 (s, C-N), 1063 (s, C-Si), 939 (s, C=C), 807 (s, C-CH₃), 519 (s, C-CH₃).

HRMS (EI) calcd for C₅H₈O₃Si (465.66): 465.2124; found: 465.2123.

5-[3-[4-(1,3-Dioxan-2-yl)phenyl]-1-methyl-3-phenylpropa-1,2-dienyl]-2-(trimethylsilyl)pyridine (18)

This compound was obtained from ZnCl₂ (2.0 M solution in THF; 0.2 mL, 0.4 mmol), PhMgCl (2.0 M solution in THF; 0.2 mL, 0.4 mmol), Pd(PPh₃)₄ (7 mg, 0.006 mmol) in THF (0.5 mL), and 2-[1-acetoxy-3-[4-(1,3-dioxan-2-yl)phenyl]-1-methylprop-2-ynyl]-5-(trimethylsilyl)pyridine (69 mg, 0.15 mmol) in THF (2 mL).

Purification of the crude product by column chromatography (SiO₂; pentane–Et₂O, 1:1) furnished 18.

Yield: 51 mg (71%); orange oil.

IR (neat): 2164 (w, C=C), 1392 (w, C=C=C) cm⁻¹.

HRMS (EI) calcd for C₅H₈O₃Si (465.66): 465.2124; found: 465.2123.

HRMS (EI) calcd for C_{30}H_{31}NO_{2}Si (465.66): 465.2124; found: 465.2123.

Acknowledgement
This work was supported by the Deutsche Forschungsgemeinschaft, the European Community (COST D12/0022/99 and D24/0003/01), and the Fonds der Chemischen Industrie.

References