Eur. J. Org. Chem. **2005** · © WILEY-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2005 · ISSN 1434–193X

SUPPORTING INFORMATION

Title: A Metathesis Approach to Aromatic Heterocycles
Author(s): Timothy J. Donohoe,* Allan J. Orr, Katherine Gosby, Matilda Bingham
Ref. No.: O200500113

General

THF was dried prior to use by distillation from sodium-benzophenone ketyl under an atmosphere of argon or by alumina column[1]. CH_2Cl_2 and MeCN were dried prior to use by distillation from calcium hydride under an atmosphere of argon or by alumina column. Ether and benzene were both dried prior to use by alumina column. Et_3N was dried by stirring over and distilling from calcium hydride and was stored over calcium hydride granules. Reagents obtained from commercial suppliers were used directly as supplied or following purification according to procedures described by Perrin and Armarego[2]. All non-aqueous reactions were carried out under an atmosphere of argon using oven- or flame- dried glassware.

Flash column chromatography was performed using silica gel 60 (0.040-0.063 mm) (Merck). Thin layer chromatography was performed on commercially available pre-coated glass-backed plates (Merck silica Kieselgel $60F_{254}$). Spots were made visible either by the quenching of UV fluorescence or by staining with a potassium permanganate solution.

^1H NMR spectra were recorded on a Bruker AVANCE AV400 (400 MHz) spectrometer in $CDCl_3$, C_6D_6, $(D_3C)_2SO$ or CD_3CN and referenced to residual solvent peaks or to $SiMe_4$ as an internal standard. Signal positions were recorded in δ ppm with the abbreviations s, d, dd, ddd, dddd, t, dt, td, q, br., app. and m denoting singlet, doublet, double doublet,

double doublet of doublets, double double doublet of doublets, triplet, doublet of triplets, triplet of doublets, quartet, broad, apparent and multiplet respectively. ^{13}C NMR spectra were recorded on the same spectrometer listed above at 100 MHz and were referenced in the same way. All NMR chemical shifts are quoted in ppm. All coupling constants, *J*, are quoted in Hz.

Infra-red spectra were recorded on a Bruker Tensor 27 Ft-IR spectrometer. Spectra were analysed either as thin films between NaCl plates or as KBr disks.

Mass spectra (*m/z*) and accurate mass data (HRMS) under the conditions of electrospray ionisation (ESI), field ionisation (FI), chemical ionisation (CI) and electron impact (EI) were recorded as detailed in Appendix 1.

Melting points were obtained using a Leica VMTG heated-stage microscope and are uncorrected.

"Petrol" refers to the fraction of petroleum ether boiling in the range 40-60 °C unless otherwise stated. "Ether" refers to diethyl ether unless otherwise stated. Known compounds were correlated with literature data which is referenced herein.

General Procedures

Method A: Oxy- and amidopalladation of methoxyallene

To a flask containing a solution of sulfonamide or alcohol in acetonitrile (0.3 M) was added Et_3N (1.5 equiv.), $Pd(OAc)_2$ (5 mol %), dppp (5 mol %) and methoxyallene (3 equiv.). The mixture was heated to reflux for 16 h before being cooled to room temperature. Et_3N (5 mL) was added to the mixture before the reaction was quenched with water (20 mL). The

product was extracted into ether (20 mL), separated and the aqueous re-extracted with ether (20 mL). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The resultant crude oils were purified by column chromatography as indicated.

Method B: Amidopalladation of methoxyallene with *in situ* trapping of phenyl iodide

To a solution of sulfonamide in toluene (0.3 M) was added iodobenzene (1 equiv.), $Pd(PPh_3)_4$ (5 mol %), K_2CO_3 (2 equiv.) and methoxyallene (3 equiv.). The reaction mixture was heated to reflux for 16 h before being cooled to room temperature. Et_3N (5 mL) was added to the mixture before quenching with water (20 mL). The organic phase was separated and re-extracted with ether (20 mL) before the combined organics were dried over Na_2SO_4 and concentrated *in vacuo*. The resultant crude materials were purified by column chromatography as indicated.

Method C: Ring Closing Metathesis

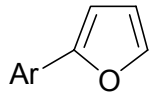
The allylic acetal was dissolved in deoxygenated dichloromethane (deoxygenated by bubbling Argon through the solvent for 30 min) in approximately 0.01 M to 0.02 M solutions. The mixture was heated to reflux for the indicated time before being cooled to room temperature and stirred openly to air for 16 h to destroy the active catalyst. The solvent was removed *in vacuo* and the ring closed products were purified by column chromatography on silica gel.

Method D: Aromatisation of ring closed intermediates

TFA (0.6 equiv.) was added to a solution of ring closed intermediate in CH_2Cl_2 and stirred at room temperature until

reaction complete. The mixture was diluted with diethyl ether (15 mL) and washed with saturated aqueous $NaHCO_3$ (15 mL). The organic layer was separated, dried over $MgSO_4$, and concentrated *in vacuo*. The aromatic products were purified by column chromatography as indicated.

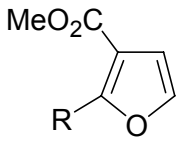
2-(4-Methoxy-phenyl)-furan **4**[3]



Ar= *p*-$MeOC_6H_4$

Acetal **2** (500 mg, 2.1 mmol) was reacted according to General Method C for 2 h, then General Method D for 5 min. Chromatography on silica gel (9:1 petrol:EtOAc) afforded **4** as an off white solid (290 mg, 79%); m.p 42- 44 °C; δ_H(400MHz; $CDCl_3$) 7.65 (2H, d, *J* 8.6, Ar), 7.46 (1H, dd, *J* 1.0, *J'* 0.7, $\mathbf{H}_5$), 6.96 (2H, d, *J* 8.0, Ar), 6.55 (1H, dd, *J* 3.3, *J'* 0.8, $\mathbf{H}_3$), 6.48 (1H, dd, *J* 3.3, *J'* 1.8 $\mathbf{H}_4$), 3.85 (3H, s, $OC\mathbf{H}_3$); δ_C($CDCl_3$) 159.0, 154.0, 141.4, 125.2, 124.0, 114.1, 111.5, 103.4, 55.3.

Methyl 2-(4-nitrophenyl)-3-furoate **10(iv)**

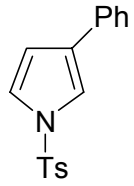


R= *p*-$NO_2C_6H_4$

Acetal **9(iv)** (360 mg, 1.2 mmol) was reacted according to General Method C for 16 h then General Method D for 3 h. Chromatography on silica gel (4:1 petrol:EtOAc) afforded **10(iv)** as a yellow solid (234 mg, 81%); m.p. 122- 124 °C; ν_{max}

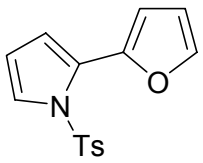
(KBr) 1713, 1516, 1343 cm^{-1}; δ_H(400MHz; $CDCl_3$) 8.30- 8.24 (4H, m, Ar), 7.54 (1H, d, *J* 1.9, $\mathbf{H}_5$), 6.91 (1H, d, *J* 1.9 , $\mathbf{H}_4$), 3.88 (3H, s, $CO_2C\mathbf{H}_3$); δ_C($CDCl_3$) 163.5, 154.5, 147.6, 142.7, 135.3, 128.8, 123.4, 116.3, 113.7, 52.0; *m/z* (CI) 247 (100, M+); HRMS (CI) $C_{12}H_{20}NO_5$ (M+) requires 247.0481, found 247.0489.

1-[(4-methylphenyl)sulfonyl]-3-phenyl-1*H*-pyrrole **18**[4]



N, *O*- acetal **17** (125 mg, 0.35 mmol) was reacted according to General Method C for 16 h, then General Method D for 10 min. Chromatography on silica gel (9:1 petrol:EtOAc) afforded **18** as a white solid (77 mg, 74%); m.p. 127- 129 °C; δ_H(400MHz; $CDCl_3$) 7.80 (2H, d, *J* 8.7), 7.47 (2H, d, *J* 8.7), 7.43 (1H, d, *J* 1.9), 7.37- 7.21 (6H, m), 6.61 (1H, d, *J* 1.7), 2.41 (3H, s, $C\mathbf{H}_3$); δ_C($CDCl_3$) 145.1, 135.9, 133.4, 130.0, 129.5, 128.8, 127.0, 126.9, 125.6, 121.6, 116.3, 112.1, 21.6.

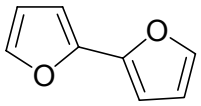
2-(2-furyl)-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrole **21**



Acetal **20** (150 mg, 0.43 mmol) was subjected to General Method C for 6 h, then General Method D for 10 min. Flash column chromatography (95:5 petrol:EtOAc) furnished **21** as a pale yellow solid (77 mg, 62 %); m.p. 49-51 °C; ν_{max} (KBr disk)/cm^{-1} 1612, 1597, 1559, 1500, 1456, 1434, 1365, 1201,

1173, 1148, 1063; δ_H(400 MHz; C_6D_6) 7.48 (1 H, app. dd, *J* 3.3, 1.8, pyrrole C^5**H**), 7.45 (2 H, d, *J* 8.3, Ts Ar**H**), 7.02 (1 H, d, *J* 1.7, furan C^5**H**), 6.75 (1 H, d, *J* 3.3, pyrrole C^3**H**), 6.51 (2 H, d, *J* 8.3, Ts Ar**H**), 6.37 (1 H, dd, *J* 3.4, 1.8, furan C^4**H**), 6.10 (1 H, dd, *J* 3.3, 1.8, pyrrole C^4**H**), 5.98 (1 H, app. t, *J* 3.4, furan C^3**H**), 1.68 (3 H, s, C$\mathbf{H}_3$); δ_C(100MHz; C_6D_6) 145.1, 144.6, 142.5, 136.4, 129.6, 127.3, 126.0, 125.0, 117.0, 112.1, 111.4, 111.3, 21.1; *m/z* (CI) 288 (100, $M+H^+$); HRMS (CI) $C_{15}H_{14}NO_3S$ requires 288.0694, found 288.0685.

[2,2']-Bifuran **24**[5]



Acetal **23** (500 mg, 1.97 mmol) was reacted according to General Method C for 3 h, and General Method D for 10 min. Chromatography on silica gel (100% petrol) afforded **24** as a colourless oil (143 mg, 54%); δ_H(400MHz; $CDCl_3$) 7.42 (2H, d, *J* 0.9, $\mathbf{H}_5$, $\mathbf{H}_5$'), 6.57 (2H, d, *J* 3.3, $\mathbf{H}_3$, $\mathbf{H}_3$'), 6.47 (2H, dd, *J* 1.7, *J'* 3.4, $\mathbf{H}_4$, $\mathbf{H}_4$'); δ_C($CDCl_3$) 146.6, 141.7, 111.3, 105.1.

REFERENCES

1. a) A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics*, **1996**, *15*, 1518; b) P. J. Alaimo, D. W. Peters, J. Arnold, R. G. Bergman, *J. Chem. Educ.*, **2001**, *78*, 64; c) D. J. Spielvogel, W. M. Davis, S. L. Buchwald, *Organometallics*, **2002**, *21*, 3833-3836.
2. *Purification of Laboratory Chemicals*; D. D. Perrin and W. L. F. Armarego, 3rd Edition, Pergamon Press, Oxford, 1988.

3. B. Schmidt, H. Wildermann, *Eur. J. Org. Chem.* **2000**, *18*, 3145.
4. P. J. Harrington, I. Sanchez, *Synth. Commun.* **1994**, *24*, 175.
5. A. R. Katritzky, J. Li, M. F. Gordeev, *J. Org. Chem.* **1993**, *58*, 3038.