N-arylated oxathiazinane heterocycles are convenient synthons for 1,3-amino ethers and 1,3-amino thioethers

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Abstract

This communication describes a variety of nucleophilic ring openings of *N*-arylated oxathiazinane heterocycles. We find that this reaction is compatible with phenoxides, naphthoxides, and thiolates and allows for the rapid assembly of *N*-aryl-amino ethers and *N*-aryl-amino thioethers. Fourteen examples are shown and a mechanistic pathway is hypothesized.

Introduction

The 1,3-amino ether and 1,3-amino thioether motifs are common in biologically active compounds, including FDA approved pharmaceuticals (Fig. 1) (Andersen et al. 2009; Chen et al. 2005). Our laboratory recently disclosed an oxidative cyclization of sulfamate esters onto alkenes to yield a variety of 6-membered *N*-arylated oxathiazinane heterocycles with pendant unsaturation (Fig. 2) (Shinde and Sathyamoorthi 2020). In our previous work, we showed one example of ring opening with sodium 2-naphthoxide. While the nucleophilic ring opening of 5-membered cyclic sulfamates (*oxathiazolidines*) with phenoxide and thiophenoxide has been extensively explored (Malhotra et al. 2015; Baraznenok et al. 2005; Carreras et al. 2007; Bower et al. 2007; Okuda and Tomioka 1994), examples of the corresponding transformation with 6-membered cyclic sulfamates (*oxathiazinanes*) remain limited (Meléndez and Lubell 2003; Atfani et al. 2001). To our knowledge, apart from the lone example in our first disclosure, this reaction has not yet been explored with *N*-arylated sulfamates. We thus sought to explore the generality of this reaction and, in this communication, we are pleased to report that the nucleophilic ring opening of diverse oxathiazinanes is possible with a variety of alkoxides, naphthoxides, phenoxides, and thiolates.

Materials and methods

General considerations

All reagents were obtained commercially unless otherwise noted. Solvents purchased from Sigma Aldrich (HPLC Grade) were used directly and without purification. Infrared (IR) spectra were recorded on a Thermo Scientific™ Nicolet™ iS™5 FT-IR Spectrometer; data are reported in frequency of absorption (cm^{-1}). NMR spectra were recorded on a Bruker Avance 400 operating at 400 and 100 MHz. ^{1}H NMR spectra were recorded at 400 MHz. Data are recorded as: chemical shift in ppm referenced internally using residue solvent peaks, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, or overlap of nonequivalent resonances), integration, coupling constant (Hz). ^{13}C NMR spectra were recorded at 100 MHz. Exact mass spectra were recorded using an electrospray ion source either in positive mode or negative mode and with a time-of-flight analyzer on a Waters LCT PremierTM mass spectrometer and are given in m/z. TLC was performed on pre-coated glass plates (Merck) and visualized either with a UV lamp (254 nm) or by dipping into a solution of $KMnO_4$–K_2CO_3 in water followed by heating. Flash chromatography was performed on silica gel (230–400 mesh). Reversed phase HPLC was performed on a Hamilton PRP-1.7 μm, 21.2 × 250 mm, C18 column.

Representative experimental procedure for nucleophilic ring opening of N-arylatedoxathiazinane heterocycles

Reactions were performed on a 0.2 mmol scale, unless otherwise specified. A 25 ml round bottom flask was charged with phenol, naphthol, or thiol nucleophile (1.3 equivalents) and 2 ml of DMF. The flask was cooled to 0 °C, and dry NaH (1.3 equivalents) was added in portions. The resulting suspension was stirred for 15–20 min. Subsequently, a solution of the oxathiazinane precursor in 1 mL of DMF was added dropwise. The reaction mixture warmed to room temperature overnight. Following this time, the reaction was quenched with 1 M HCl (2 mL) and transferred to a separatory funnel with an additional 15 mL of deionized H_2O. The aqueous mixture was subsequently basified with 1 M NaOH. Following this, the aqueous phase was extracted with three portions of ethyl acetate, the organic fractions were pooled, washed once with brine solution, and dried with Na_2SO_4. After removal of solvent under reduced pressure, the resulting residue was purified by chromatography on silica gel (gradient of 3–5% ethyl acetate in hexanes) to yield ring-opened *N*-aryl-amino ether or *N*-arylamino thioether product.

Characterization of products in Table 1 (starting materials have been fully characterized elsewhere (Shinde and Sathyamoorthi 2020))

(E)-4-Methoxy-N-(1-phenoxyhex-4-en-3-yl)aniline—(Table 1, Product Entry 1): Viscous light-yellow liquid (47 mg, 79%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.7 (ddd, J = 6.5, 1.7, 0.8 Hz, 3H), 1.9–2.2 (m, 2H), 3.6 (s, 1H), 3.8 (s, 3H), 4.0–4.2 (m, 3H), 5.4 (ddq, J = 15.4, 6.8, 1.6 Hz, 1H), 5.7 (dqd, J = 15.4, 6.5, 1.1 Hz, 1H), 6.5–6.7 (m, 2H), 6.7–6.8 (m, 2H), 6.9–7.0 (m, 3H), 7.3–7.4 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 17.8, 35.5, 54.0, 55.8, 65.1, 114.6, 114.8, 115.0, 120.8, 126.8, 129.5, 132.7, 141.8, 152.1, 158.9; FT-IR 3347, 2937, 1510, 1031, 820 cm^{-1}; HRMS calcd C$_{19}$H$_{24}$NO$_2$ 298.1807 found 298.1792 (MH+).

(E)-N-(1-(4-Ethylphenoxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 2): Viscous light-yellow liquid (52 mg, 80%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.1 (t, J = 7.6 Hz, 3H), 1.6 (ddd, J = 6.4, 1.7, 0.8 Hz, 3H), 1.8–2.0 (m, 2H), 2.5 (q, J = 7.6 Hz, 2H), 3.6 (s, 1H), 3.7 (s, 3H), 3.8–4.1 (m, 3H), 5.3 (ddq, J = 15.3, 6.7, 1.6 Hz, 1H), 5.5–5.7 (m, 1H), 6.4–6.6 (m, 2H), 6.6–6.7 (m, 2H), 6.7–6.8 (m, 2H), 7.0–7.1 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 15.9, 17.7, 28.0, 35.6, 54.1, 55.8, 65.3, 114.5, 114.8, 114.9, 126.7, 128.7, 132.7, 136.5, 141.9, 152.0, 156.9; FT-IR 3317, 2920, 1454, 1024, 764 cm^{-1}; HRMS calcd C$_{21}$H$_{28}$NO$_2$ 326.2120 found 326.2127 (MH+).

(E)-N-(1-(4-Bromophenoxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 3): Viscous light-yellow liquid (53mg, 70%); ^{1}H NMR (400MHz, CDCl$_3$) δ 1.7 (ddd, J=6.5, 1.7, 0.8 Hz, 3H), 1.9–2.2 (m, 2H), 3.4–3.7 (s, 1H), 3.8 (s, 3H), 3.9–4.2 (m, 3H), 5.4–5.5 (m, 1H), 5.7 (dtd, J=14.0, 6.5, 1.1 Hz, 1H), 6.6–6.7 (m, 2H), 6.8–6.9 (m, 4H), 7.4–7.5 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 17.8, 35.4, 53.9, 55.8, 65.5, 112.9, 114.9, 115.0, 116.4, 126.9, 132.3, 132.6, 141.7, 152.1, 158.0; FT-IR 3317, 2920, 1462, 1026, 750 cm^{-1}; HRMS calcd C$_{19}$H$_{23}$NO$_2$Br 376.0912 found 376.0959 (MH+).

(E)-N-(1-(3-Bromophenoxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 4): Viscous light-yellow liquid (53 mg, 70%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.7 (dt, J = 6.3, 1.4 Hz, 3H), 2.0 (dtdd, J = 20.6, 14.1, 6.7, 5.5 Hz, 2H), 3.6 (t, J = 18.1 Hz, 1H), 3.8 (s, 3H), 3.9–4.2 (m, 3H), 5.4 (ddq, J = 15.3, 6.8, 1.7 Hz, 1H), 5.7 (dqd, J = 15.3, 6.5, 1.1 Hz, 1H), 6.6–6.6 (m, 2H), 6.7–6.8 (m, 2H), 6.8–6.9 (m, 1H), 7.0–7.2 (m, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 17.8, 35.4, 53.8, 55.8, 65.4, 113.6, 114.9, 115.0, 117.8, 122.8, 123.9, 127.0, 130.6, 132.5, 141.7, 152.1, 159.7; FT-IR 3396, 2920, 1511, 1035, 750 cm^{-1}; HRMS calcd C$_{19}$H$_{23}$NO$_2$Br 376.0912 found 376.0887 (MH+).

(E)-N-(1-(benzo[d][1,3]dioxol-5-yloxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 5): Yellow oil (31 mg, 45%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.76–6.66 (m, 2H), 6.62 (d, J = 8.5 Hz, 1H), 6.59–6.48 (m, 2H), 6.42 (d, J = 2.5 Hz, 1H), 6.24 (dd, J = 8.5, 2.5 Hz, 1H), 5.83 (s, 2H), 5.58 (dqd, J = 15.3, 6.5, 1.1 Hz, 1H), 5.31 (ddq, J = 15.3, 6.8, 1.6 Hz, 1H), 3.92 (dddd, J = 27.8, 9.6, 6.7, 5.5 Hz, 3H), 3.66 (s, 3H), 2.04–1.82 (m, 2H), 1.59 (ddd, J = 6.4, 1.6, 0.8 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 154.34, 152.36, 148.24, 141.68, 132.27, 127.16, 115.38, 114.79, 107.95, 105.77, 101.12, 98.12, 66.12, 55.79, 54.45, 35.32, 29.71, 17.77; FT-IR 3400, 2916, 1501, 1036, 749 cm^{-1}; HRMS calcd C$_{20}$H$_{24}$NO$_4$ 342.1705 found 342.1687 (MH+).

(E)-N-(1-(4-chloro-3-methylphenoxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 6): Viscous light-yellow liquid (26 mg, 43%); ^{1}H NMR (400 MHz, CDCl$_3$) 7.21 (d, J = 8.7 Hz, 1H), 6.78–6.76 (m, 2H), 6.75–6.73 (m, 1H), 6.67 (ddd, J = 8.8, 3.0, 0.6 Hz, 1H), 6.61–6.55 (m, 2H), 5.65 (dtd, J = 15.3, 6.5, 1.0 Hz, 1H), 5.43–5.32 (m, 1H), 4.10–3.93 (m, 3H), 3.74 (s, 3H), 2.33 (s, 3H), 2.07–1.95 (m, 2H), 1.67 (ddd, J = 6.5, 1.6, 0.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.5, 152.2, 141.8, 137.1, 132.7, 129.7, 126.9, 126.0, 117.2, 115.1, 114.9, 113.3, 65.6, 55.9, 54.0, 35.6, 20.4, 17.9; FT-IR 3395, 2931, 1509, 1038, 818 cm^{-1}; HRMS calcd C$_{20}$H$_{25}$ClNO$_2$ 346.1574 found 346.1565 (MH+).

(E)-N-(1-(3,4-dimethylphenoxy)hex-4-en-3-yl)aniline—(Table 1, Product Entry 7): Viscous light-yellow liquid; Yield: (45 mg, 78%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.18–7.10 (m, 2H), 7.02 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 2.8 Hz, 1H), 6.69–6.57 (m, 4H), 5.74–5.61 (m, 1H), 5.45–5.35 (m, 1H), 4.13–3.97 (m, 3H), 3.93 (s, 1H), 2.23 (s, 3H), 2.19 (s, 3H), 2.03 (dtd, J = 7.4, 6.6, 5.4 Hz, 2H), 1.67 (ddd, J = 6.4, 1.6, 0.7 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.1, 147.8, 137.8, 132.5, 130.4, 129.2, 128.9, 126.8, 117.2, 116.3, 113.6, 111.7, 65.3, 53.2, 35.7, 20.2, 18.9, 17.9; FT-IR 3403, 3050, 2917, 1501, 1049, 748 cm^{-1}; HRMS calcd C$_{20}$H$_{26}$NO 296.2014 found 296.2006 (MH+).

(E)-N-(1-((6-bromonaphthalen-2-yl)oxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 8): Light Brown Solid (34 mg, 40%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, J = 1.9 Hz, 1H), 7.57 (d, J = 8.9 Hz, 1H), 7.48 (d, J = 8.7 Hz, 1H), 7.41 (dd, J = 8.7, 2.0 Hz, 1H), 7.10 (dd, J = 9.0, 2.5 Hz, 1H), 7.00 (d, J = 2.6 Hz, 1H), 6.70–6.63 (m, 2H), 6.62–6.39 (m, 2H), 5.60 (dqd, J = 15.4, 6.5, 1.1 Hz, 1H), 5.34 (ddq, J = 15.3, 6.8, 1.6 Hz, 1H), 4.23–3.85 (m, 3H), 3.65 (s, 3H), 2.15–1.89 (m, 2H), 1.60 (ddd, J = 6.5, 1.7, 0.8 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.12, 152.17, 141.61, 133.06, 132.53, 130.05, 129.66, 129.62, 128.52, 128.39, 126.95, 119.96, 117.06, 115.06, 114.84, 106.76, 65.28, 55.81, 54.01, 35.43, 17.78. FT-IR 3355, 2929, 1510, 1016, 817 cm^{-1}; HRMS calcd C$_{23}$H$_{25}$BrNO$_2$ 426.1069 found 426.1059 (MH+).

Ethyl (E)-4-((1-(naphthalen-1-yloxy)hex-4-en-3-yl)amino) benzoate—(Table 1, Product Entry 9): Done on 0.167 mmol scale; Viscous light-yellow liquid (54.5 mg, 70%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.4 (t, J = 7.1 Hz, 3H), 1.7 (ddd, J = 6.6, 1.7, 0.9 Hz, 3H), 2.3 (tdd, J = 6.4, 4.9, 3.7 Hz, 2H), 4.2–4.4 (m, 5H), 4.6 (d, J = 6.6 Hz, 1H), 5.5 (ddq, J = 15.3, 6.4, 1.6 Hz, 1H), 5.7–5.8 (m, 1H), 6.6 (dq, J = 9.8, 2.7, 2.3 Hz, 2H), 6.8 (dd, J = 7.6, 1.0 Hz, 1H), 7.3–7.4 (m, 1H), 7.5 (d, J = 8.2 Hz, 1H), 7.5–7.6 (m, 2H), 7.8–7.9 (m, 3H), 8.3 (ddd, J = 6.2, 3.4, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 14.5, 17.7, 35.2, 52.9, 60.1, 65.1, 104.8, 112.1, 118.7, 120.6, 121.7, 125.4, 125.6, 125.8, 126.5, 127.6, 127.7, 131.1, 131.4, 134.6, 151.2, 154.3, 166.8; FT-IR 3374, 2933, 1694, 1510, 1036, 753 cm^{-1}; HRMS calcd C$_{25}$H$_{28}$NO$_3$ 390.2069 found 390.2084 (MH+).

(E)-N-(1-(benzyloxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 10): Yellow oil (25.8 mg, 43%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32–7.20 (m, 5H), 6.72–6.63 (m, 2H), 6.56–6.46 (m, 2H), 5.53 (dqd, J = 15.4, 6.4, 1.1 Hz, 1H), 5.28 (ddq, J = 15.3, 6.7, 1.6 Hz, 1H), 4.42 (d, J = 1.1 Hz, 2H), 3.86–3.73 (m, 1H), 3.66 (s, 3H), 3.53 (dddd, J = 28.3, 9.5, 6.6, 5.3 Hz, 2H), 1.80 (qd, J = 6.6, 5.1 Hz, 2H), 1.57 (ddd, J = 6.5, 1.7, 0.8 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 152.12, 141.47, 138.35, 132.61, 128.40, 127.70, 127.63, 126.59, 115.17, 114.74, 73.11, 67.68, 55.81, 54.90, 35.74, 17.73; FT-IR 3383, 2916, 1510, 1036, 748 cm^{-1}; HRMS calcd for C$_{10}$H$_{26}$NO$_2$ 312.1964 found 312.1936 (MH+).

(E)-N-(1-((4-methoxybenzyl)oxy)hex-4-en-3-yl)aniline—(Table 1, Product Entry 11): Viscous light-yellow liquid (28 mg, 47%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.26–7.24 (m, 2H), 7.17–7.11 (m, 2H), 6.90–6.85 (m, 2H), 6.69–6.64 (m, 1H), 6.60–6.56 (m, 2H), 5.63 (dqd, J = 15.3, 6.4, 1.1 Hz, 1H), 5.36 (ddq, J = 15.3, 6.3, 1.6 Hz, 1H), 4.43 (s, 2H), 4.11 (s, 1H), 3.97 (q, J = 6.8, 6.4 Hz, 1H), 3.82 (s, 3H), 3.59 (dddd, J = 28.3, 9.5, 6.6, 5.2 Hz,

2H), 1.87 (tdd, $J = 6.6$, 5.2, 4.0 Hz, 2H), 1.66 (ddd, $J = 6.5$, 1.7, 0.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 159.3, 148.0, 132.8, 130.6, 129.4, 129.2, 126.3, 116.9, 113.9, 113.4, 72.9, 67.5, 55.4, 53.6, 36.0, 17.8; FT-IR 3394, 2915, 1509, 1094, 748 cm^{-1}; HRMS calcd for C$_{20}$H$_{26}$NO$_2$ 312.1964 found 312.1942 (MH+).

(E)-N-(1-(2-Aminophenoxy)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 12): Viscous light-yellow liquid (36 mg, 58%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.7 (ddd, $J = 6.4$, 1.7, 0.9 Hz, 3H), 2.0–2.2 (m, 2H), 3.7 (s, 5H), 4.0 (q, $J = 6.6$ Hz, 1H), 4.1–4.2 (m, 2H), 5.4 (ddq, $J = 15.3$, 6.7, 1.6 Hz, 1H), 5.7 (dqd, $J = 15.4$, 6.5, 1.1 Hz, 1H), 6.6–6.7 (m, 2H), 6.7–6.9 (m, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 13 C NMR (101 MHz, CDCl3) δ 17.8, 35.6, 54.0, 55.8, 65.6, 112.0, 114.8, 115.0, 115.2, 118.5, 121.4, 126.8, 132.7, 136.4, 141.7, 146.5, 152.1; FT-IR 3383, 2938, 1509, 1038, 819 cm^{-1}; HRMS calcd for C$_{19}$H$_{25}$N$_2$O$_2$ 313.1916 found 313.1884 (MH+).

(E)-4-methoxy-N-(1-(phenylthio)hex-4-en-3-yl)aniline—(Table 1, Product Entry 13): Yellow oil (54 mg, 70%); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.25 (dt, $J = 8.3$, 1.1 Hz, 2H), 7.19 (d, $J = 7.5$ Hz, 2H), 7.09 (d, $J = 6.7$ Hz, 1H), 6.84–6.61 (m, 2H), 6.59–6.42 (m, 2H), 5.61–5.50 (m, 1H), 5.24 (ddt, $J = 15.4$, 7.0, 1.5 Hz, 1H), 3.80 (q, $J = 6.8$ Hz, 1H), 3.66 (s, 3H), 3.00–2.85 (m, 2H), 1.90–1.71 (m, 2H), 1.59 (dd, $J = 6.5$, 1.6 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 152.40, 140.91, 136.36, 132.08, 129.24, 128.92, 127.44, 125.98, 115.43, 114.80, 55.79, 35.08, 30.32, 29.72, 17.79; FT-IR 3372, 2917, 1510, 1038, 819 cm^{-1}; HRMS calcd for C$_{19}$H$_{24}$NOS 314.1579 found 314.1580 (MH+).

(*E*)-*N*-(1-(*tert*-butylthio)hex-4-en-3-yl)-4-methoxyaniline—(Table 1, Product Entry 14): Viscous light-yellow liquid (36 mg, 70%); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.75 (d, $J = 8.9$ Hz, 2H), 6.58 (d, $J = 9.0$ Hz, 2H), 5.65 (dqd, $J = 15.4$, 6.5, 1.1 Hz, 1H), 5.32 (ddq, $J = 15.3$, 6.9, 1.6 Hz, 1H), 3.83 (q, $J = 6.7$ Hz, 1H), 3.74 (s, 3H), 3.36 (s, 1H), 2.61 (t, $J = 7.4$ Hz, 2H), 1.86–1.72 (m, 2H), 1.67 (ddd, $J = 6.5$, 1.7, 0.7 Hz, 3H), 1.31 (s, 9H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 152.2, 141.9, 132.8, 126.9, 115.1, 114.9, 56.0, 42.3, 36.1, 31.1, 25.1, 17.9; FT-IR 3364, 2957, 1510, 1039, 818 cm^{-1}; HRMS calcd C$_{17}$H$_{28}$NOS 294.1892 found 294.1902 (MH+).

Results and discussion

We conducted a systematic exploration of oxathiazinane heterocycles with various O$^-$ and S$^-$ nucleophiles. We were pleased to find that ring opening with sodium phenoxide proceeded with high efficiency (Table 1, Entry 1); the reaction with sodium 4-ethylphenoxide (Table 1, Entry 2) was similarly successful. Opening with sodium 4-bromophenoxide provided product with a slightly lower yield (Table 1, Entry 3); we were somewhat surprised to observe that transposing the bromide to the meta position (Table 1, Entry 4) did not affect the reaction. With sesamol (Table 1, Entry 5) and 4-chloro-3-methylphenol (Table 1, Entry 6), the efficiency of the reaction dropped, but the amino ether product still formed in synthetically useful yields. We were not confined to ring opening of *N*-4-methoxyphenyl oxathiazinane heterocycles. Opening of an *N*-phenyl oxathiazinane (Table 1, Entries 7 and 11) as well as an *N*-4-ethoxycarbonyl oxathiazinane (Table 1, Entry 9) was also possible. Further, in addition to sodium aryloxides, sodium alkoxides

(benzyloxide and 4-methoxybenzyloxide) were competent nucleophiles (Table 1, Entries 10 and 11). We envision that these benzyl groups may be facilely removed (Ghosh and Kulkarni 2020; Llàcer et al. 2006) to yield valuable *N*-aryl-amino alcohol molecules. With 2-aminophenol, we observed product solely from O$^-$ attack (Table 1, Entry 12). To our delight, ring opening with aryl and alkylthiols was both possible and efficient (Table 1, Entries 13 and 14).

Our proposed mechanism (Fig. 3) takes inspiration from what has been postulated for analogous nucleophilic openings of oxathiazolidines (Meléndez and Lubell 2003). NaH deprotonation of phenol forms phenoxide which then selectively cleaves the C–O bond of the oxathiazinane heterocycle in a nucleophilic displacement. During acidic workup, SO$_3$ is liberated and the resulting aryl nitrogen anion is quenched.

Conclusion

We have presented our findings on the nucleophilic ring openings of *N*-arylated oxathiazinane heterocycles with phenoxides, naphthoxides, and thiolates. Based on our investigations, we postulate this to be a fairly general reaction for the rapid assembly of *N*-aryl-amino ethers and *N*-aryl-amino thioethers. We hope that this work contributes to the rising importance of the oxathiazinane heterocycle in synthetic organic chemistry.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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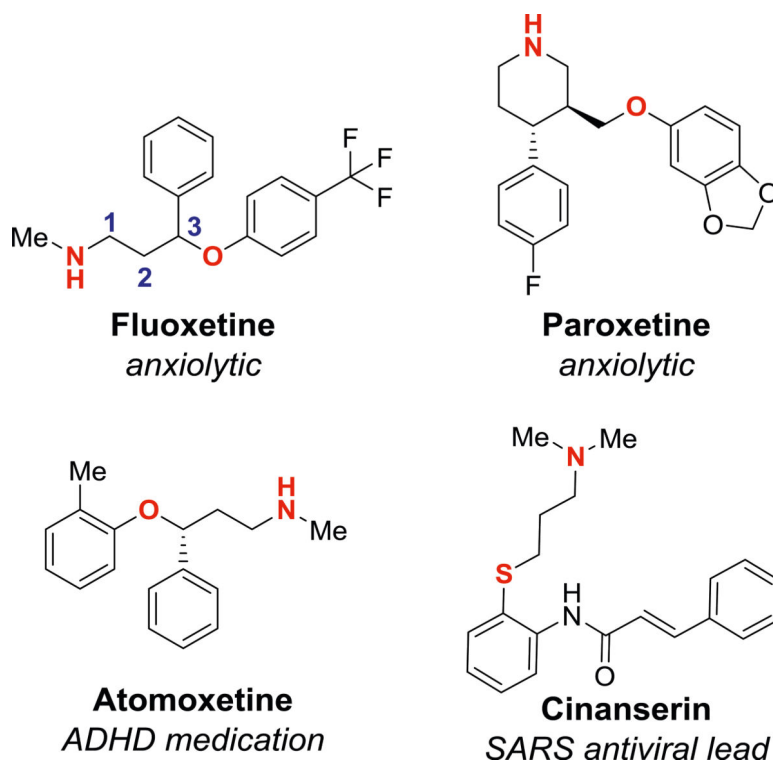
Fig. 1.
1,3-amino ethers and 1,3-amino thioethers are vital motifs in clinically approved
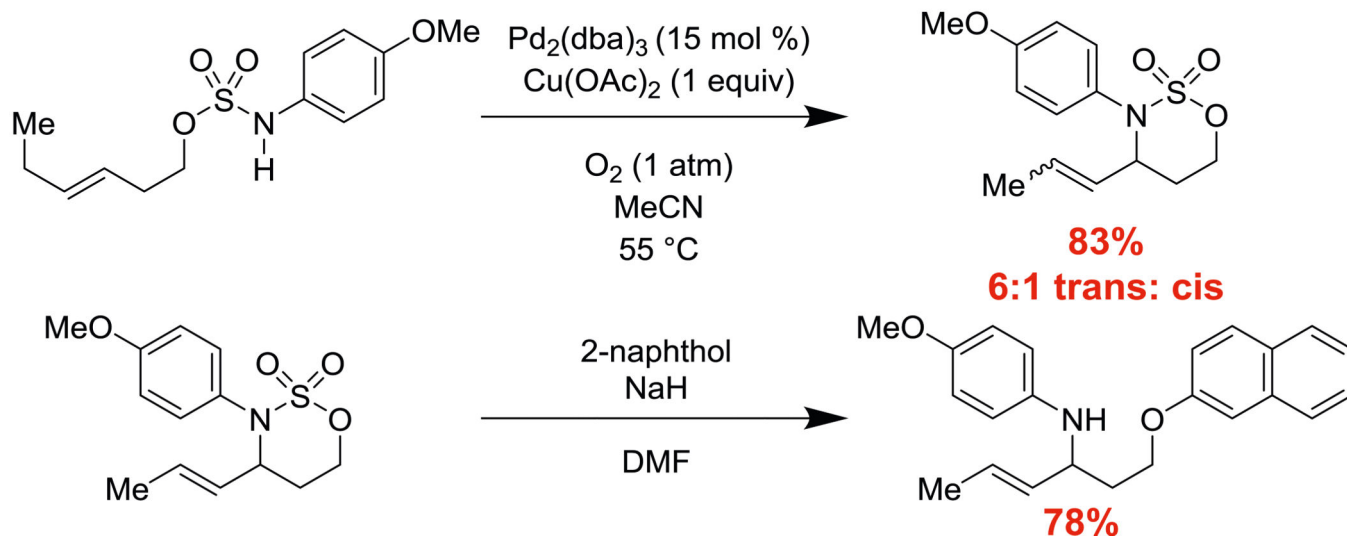pharmaceutics

Sathyamoorthi and Shinde (2020)

Fig. 2.
a An aza-Wacker cyclization of alkenyl sulfamate esters. **b** Lone example of naphthoxide opening of an N-aryl oxathiazinane heterocycle
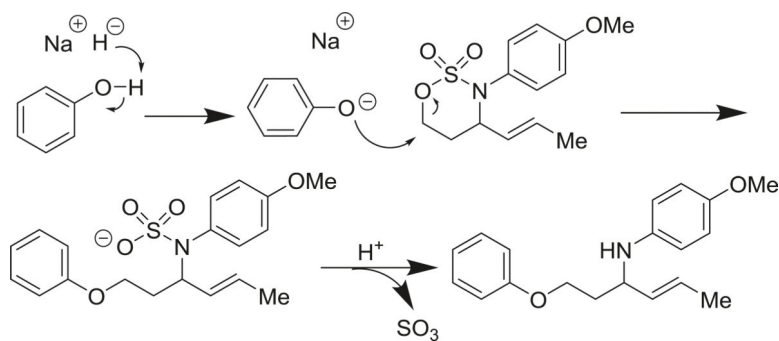
Fig. 3.
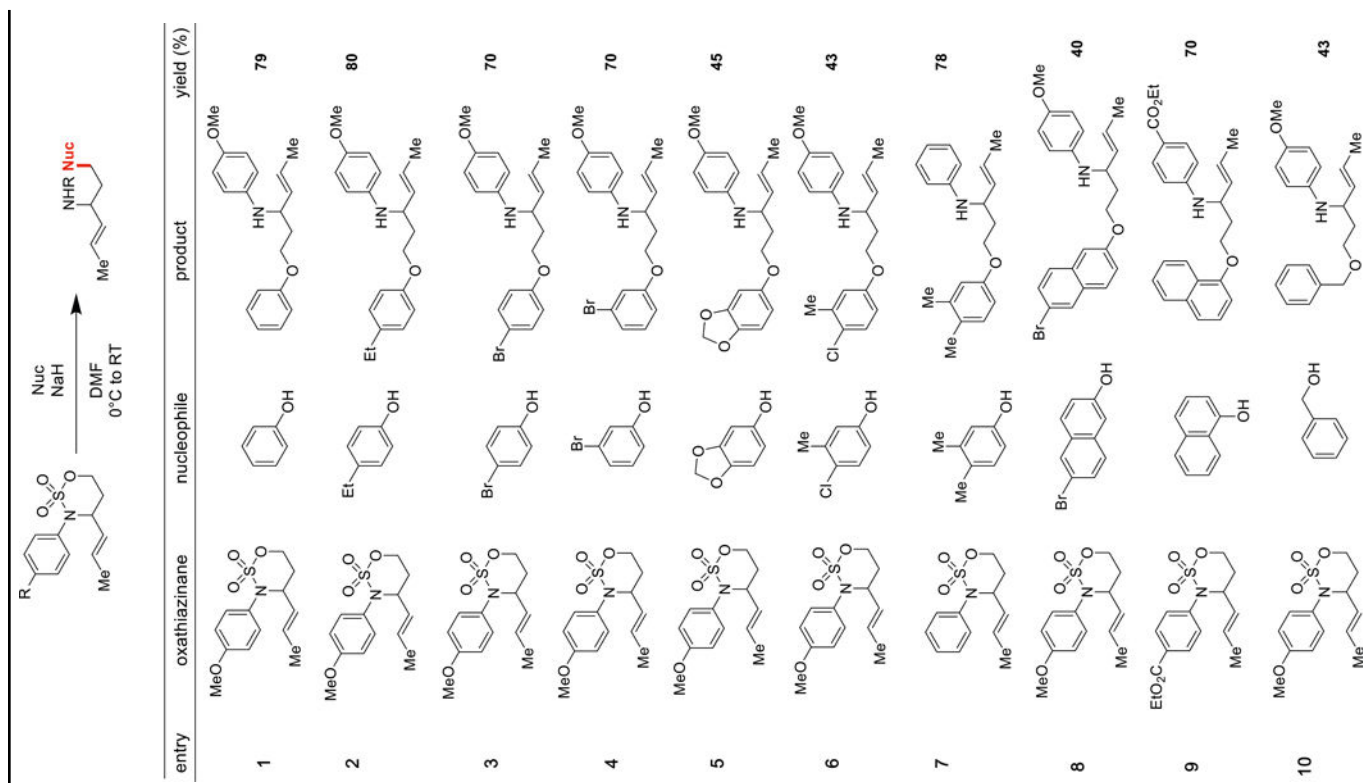Proposed mechanism for nucleophilic ring opening of *N*-aryl-oxathiazinane heterocycles

Table 1

Scope of oxathiazinane heterocycle and nucleophile