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Nitration-Oximization of Styrene Derivatives with *tert*-Butyl Nitrite: Synthesis of *α*-Nitrooximes

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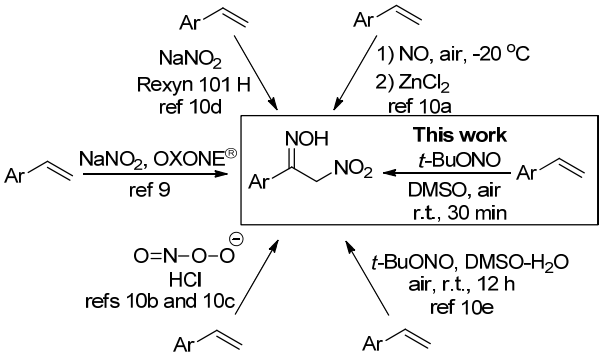
A highly efficient method for direct nitration-oximization of styrene derivatives using *tert*-butyl nitrite (*t*-BuONO) in DMSO was developed. The present method offers a convenient and practical approach for the synthesis of *α*-nitrooximes in moderate to high yields. The salient features entail mild reaction conditions, metal-free reagent, environmentally benign solvent and simple experimental procedure.

Keywords *α*-nitrooximes, *tert*-butyl nitrite, nitration-oximization, styrenes

Introduction

The development of environmentally friendly and operationally simple synthetic methods for the construction of functionalized molecules receives continuous attention in modern organic synthesis.[1] Therefore, chemists aim to develop green and sustainable procedures, such as heterogeneous catalysis,[2] metal-free synthesis[3] or catalyst-free synthesis.[4] In particular, metal-free synthetic protocols which avoid the utilization of any metals have been extensively studied as the alternatives to reactions mediated by toxic, expensive and difficult to handle metallic reagents. Additionally, the metal residue and environmental pollution are usually the important problem caused by metal-mediated transformations. Vicinal diamines exist in many naturally occurring and biologically active compounds and exhibit as important building blocks and ligands in the field of asymmetric synthesis.[5] Therefore, a number of research efforts have been devoted to devise convenient methods for vicinal diamine syntheses.[6] Among those, direct diamination of alkenes is clearly a powerful route to construct vicinal diamine scaffolds.[7] As a part of our ongoing interest in the development of new methodology towards difunctionalization of alkenes and alkynes,[8] we recently disclosed OXONE® mediated *α*-nitrooximes synthesis employing $NaNO_2$ in aqueous acetonitrile (Scheme 1).[9] The method while offering a direct method for preparation of *α*-nitrooximes from styrene derivatives had several limitations including requirement of excess quantities of reagents, poor results with electron-releasing substituted styrene derivatives and portion-wise addition of a reagent. Notably, from a practical aspect, metal-free syntheses are preferable, as the reaction under metal-free conditions would be of great importance to the pharmaceutical fields. Therefore, a related set of transformations would be of particular interest, if it can be carried out under metal-free conditions without lowering the reaction efficiency. It is worth to note here that limited works toward the realm of *α*-nitrooxime synthesis were published.[10] During a process of preparation this manuscript, a report on the use of *t*-BuONO in a mixture of DMSO-water (2∶1, *V*∶*V*), r.t., 12 h for *α*-nitrooxime synthesis of styrene derivatives was disclosed by Tan and co-workers.[10e] This prompts us to report our findings. We report herein that a range of styrene derivatives, vinyl-substituted heteroaromatics as well as 1-aryl-1,3-butadienes can readily undergo nitration-oximization employing *t*-BuONO in DMSO under an air atmosphere at room temperature for 30 min to yield their corresponding

Scheme 1 Nitration-oximization of styrene derivatives



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α-nitrooximes (Scheme 1). The method offers experimental simplicity, practical and facile method, using non-metallic reagents under mild and facile reaction conditions.

Experimental

General

^{1}H NMR spectra were recorded with a Bruker DPX-300 (300 MHz) or a Bruker Ascend™ 400 (400 MHz) spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard or in acetone-d_6 using a residual non-deuterated solvent peak as an internal standard. ^{13}C NMR spectra were recorded with a Bruker DPX-300 (75 MHz) or a Bruker Ascend™ 400 (100 MHz) spectrometer in $CDCl_3$ or acetone-d_6 using a residual non-deuterated solvent peak as an internal standard. IR spectra were recorded with a Perkin Elmer 683 GX FTIR System spectrometer. High resolution mass spectra were recorded with a Bruker micro TOF spectrometer. Melting points were recorded with a digital Electrothermal Melting 9100 apparatus and uncorrected. Column chromatography was performed using Merck silica gel (Art 7734). Other common solvents (dichloromethane, hexanes, ethyl acetate, and acetone) were distilled before use.

General procedure for the synthesis of α-nitrooximes

tert-Butyl nitrite (103.1 mg, 0.12 mL, 1 mmol) was added to a solution of the substrate (0.5 mmol) in dimethylsulfoxide (2.5 mL). The solution was stirred under an air atmosphere at room temperature (32－35 ℃) for 30 min. Then the reaction solution was quenched by the addition of water (5 mL) and was extracted with EtOAc (15 mL×3). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried (anhydrous $MgSO_4$), filtered and vacuumed (aspirator). The residue was purified by column chromatography (SiO_2) using acetone/hexanes as the eluent to afford the corresponding product.

1-(4-Bromophenyl)-2-nitroethanone oxime (**2a**):[9] White solid (112.6 mg, 87% yield). m.p. 97－98 ℃ (CH_2Cl_2/hexanes); ^{1}H NMR (400 MHz, acetone-d_6) δ: 11.67 (s, 1H), 7.75 (d, J=8.6 Hz, 2H), 7.63 (d, J=8.6 Hz, 2H), 5.89 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 147.2 (C), 133.5 (C), 131.8 (2×CH), 127.9 (2×CH), 123.4 (C), 68.0 (CH_2); IR (KBr) ν: 3232 (O－H), 1636 (C=N), 1558 and 1375 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_8BrN_2O_3$ $[M+H]^+$ 258.9718, found 258.9719.

1-(4-Chlorophenyl)-2-nitroethanone oxime (**2b**):[10d] Yellow viscous oil (79.8 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.18 (br s, 1H), 7.56 (d, J=8.5 Hz, 2H), 7.41 (d, J=8.5 Hz, 2H), 5.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.7 (C), 136.7 (C), 131.4 (C), 129.4 (2×CH), 127.5 (2×CH), 68.2 (CH_2); IR (KBr) ν: 3235 (O－H), 1596 (C=N), 1562 and 1379 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_8ClN_2O_3$ $[M+H]^+$ 215.0223, found 215.0213.

1-(3-Chlorophenyl)-2-nitroethanone oxime (**2c**):[9] Yellow viscous oil (80.1 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$, isomeric ratio 13.3∶1, minor isomer marked *) δ: 9.53 (br s, 1H of major and minor isomers), 7.63 (t, J=1.6 Hz, 1H of major and minor isomers), 7.48－7.34 (m, 3H of major and minor isomers), 5.62 (s, 1.86H), 5.39* (s, 0.14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.5 (C), 135.1 (C), 134.7 (C), 130.5 (CH), 130.3 (CH), 130.0* (CH), 128.5* (CH), 126.3 (CH), 126.2* (CH), 124.3 (CH), 77.8* (CH_2), 68.2 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) ν: 3274 (O－H), 1630 (C=N), 1559 and 1373 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_7ClN_2NaO_3$ $[M+Na]^+$ 237.0043, found 237.0041.

1-(2-Chlorophenyl)-2-nitroethanone oxime (**2d**):[9] Yellow viscous oil (64.8 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$, isomeric ratio 1.6∶1, minor isomer marked *) δ: 9.50 (br s, 0.59H), 8.78* (br s, 0.35H), 7.53－7.34 (m, 4H of major and minor isomers), 5.60 (s, 1.24H), 5.42* (s, 0.76H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.9 (C), 148.0* (C), 132.6 (C), 132.5* (C), 131.7 (CH), 131.5 (CH), 131.2* (CH), 130.7* (CH), 130.0 (CH), 129.8* (CH), 129.6 (C), 127.5 (CH), 127.1* (CH), 77.4* (CH_2), 70.2 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (neat) ν: 3272 (O－H), 1622 (C=N), 1558 and 1373 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_7ClN_2NaO_3$ $[M+Na]^+$ 237.0043, found 237.0042.

1-(4-Fluorophenyl)-2-nitroethanone oxime (**2e**):[10d] Yellow viscous oil (71.2 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$, isomeric ratio 8.5∶1, minor isomer marked *) δ: 9.67 (br s, 0.83H), 9.35* (br s, 0.10H), 7.59 (dd, J=8.6, 4.6 Hz, 2H of major and minor isomers), 7.11 (dd, J=8.6, 4.6 Hz, 2H of major and minor isomers), 5.62 (s, 1.79H), 5.40* (s, 0.21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.0 (d, J=250.4 Hz, C), 163.4* (d, J=250.4 Hz, C), 147.8 (d, J=12.5 Hz, C), 130.7 (d, J=8.6 Hz, 2×CH), 129.1 (d, J=3.2 Hz, C), 128.3* (d, J=8.6 Hz, 2×CH), 116.3 (d, J=21.8 Hz, 2×CH), 115.9* (d, J=21.8 Hz, 2×CH), 78.0* (CH_2), 68.6 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) ν: 3279 (O－H), 1602 (C=N), 1549 and 1376 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_7FN_2NaO_3$ $[M+Na]^+$ 221.0338, found 221.0337.

1-(3-Fluorophenyl)-2-nitroethanone oxime (**2f**):[9] Yellow viscous oil (72.8 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$, isomeric ratio 26.9∶1, minor isomer marked *) δ: 9.28 (br s, 1H of major and minor isomers), 7.44－7.36 (m, 3H of major and minor isomers), 7.18－7.13 (m, 1H of major and minor isomers), 5.63 (s, 1.88H), 5.40* (s, 0.07H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0 (d, J=245.9 Hz, C), 147.6 (d, J=2.4 Hz, C), 135.1 (d, J=7.9 Hz, C), 130.7 (d, J=8.3 Hz, CH), 130.4* (d, J=8.3 Hz, CH), 123.7* (d, J=3.0 Hz, CH),

121.9 (d, J=3.0 Hz, CH), 117.5 (d, J=21.2 Hz, CH), 115.9* (d, J=23.3 Hz, CH), 113.3 (d, J=23.3 Hz, CH), 77.9* (CH_2), 68.2 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3274 (O−H), 1610 (C=N), 1558 and 1376 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_8H_7FN_2NaO_3$ $[M + Na]^+$ 221.0338, found 221.0331.

1-(4-Nitrophenyl)-2-nitroethanone oxime (**2g**):[9] Pale yellow solid (70.2 mg, 62% yield). m.p. 123−124 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 21.2∶1, minor isomer marked *) δ: 12.15 (s, 1H of major and minor isomers), 8.31 (d, J=9.0 Hz, 2H of major and minor isomers), 8.08 (d, J=9.0 Hz, 2H of major and minor isomers), 5.98 (s, 1.91H), 5.78* (s, 0.09H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 148.4 (C), 146.8 (C), 140.4 (C), 130.0* (2×CH), 127.1 (2×CH), 123.8 (2×CH), 123.3* (2×CH), 77.9* (CH_2), 67.9 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3364 (O−H), 1599 (C=N), 1567 and 1380 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_8H_7N_3NaO_5$ $[M+Na]^+$ 248.0283, found 248.0282.

1-(3-Nitrophenyl)-2-nitroethanone oxime (**2h**):[9] Pale yellow solid (74.0 mg, 66% yield). m.p. 98−99 ℃ (CH_2Cl_2/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 20.6∶1, minor isomer marked *) δ: 12.09 (s, 1H of major and minor isomers), 8.62 (s, 1H of major and minor isomers), 8.30 (dd, J=8.0, 1.3 Hz, 1H of major and minor isomers), 8.22 (d, J=8.0 Hz, 1H of major and minor isomers), 7.76 (t, J=8.0 Hz, 1H of major and minor isomers), 6.00 (s, 1.85H), 5.82* (s, 0.09H); ^{13}C NMR (100 MHz; acetone-d_6) δ: 148.6 (C), 146.6 (C), 136.1 (C), 134.8* (CH), 132.0 (CH), 130.2 (CH), 129.8* (CH), 124.2* (CH), 124.0 (CH), 123.6* (CH), 120.6 (CH), 77.9* (CH_2), 67.9 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3314 (O−H), 1575 (C=N), 1533 and 1378 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_8H_7N_3NaO_5$ $[M+Na]^+$ 248.0283, found 248.0276.

Methyl-4-(1-(hydroxyimino)-2-nitroethyl)benzoate (**2i**): Yellow viscous oil (73.5 mg, 60% yield). ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 27.6∶1, minor isomer marked *) δ: 11.89 (br s, 1H of major and minor isomers), 8.07 (d, J=8.5 Hz, 2H of major and minor isomers), 7.93 (d, J=8.5 Hz, 2H of major and minor isomers), 5.94 (s, 1.93H), 5.73* (s, 0.07H), 3.91 (s, 3H of major and minor isomers); ^{13}C NMR (100 MHz, acetone-d_6) δ: 165.9 (C), 147.3 (C), 138.5 (C), 130.9 (C), 129.6 (2×CH), 129.2* (2×CH), 128.8* (2×CH), 126.1 (2×CH), 68.0 (CH_2), 51.7* (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3399 (O−H), 1716 (C=O), 1608 (C=N), 1561 and 1380 (NO_2) cm^{-1}; MS m/z (%) relative intensity 238 (M^+, 3), 191 (8), 161 (90); HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2NaO_5$ $[M+Na]^+$ 261.0487, found 261.0488.

3-(1-(Hydroxyimino)-2-nitroethyl)benzaldehyde (**2j**):[9] Yellow solid (69.4 mg, 66% yield). m.p. 118−119 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6) δ: 11.83 (s, 1H), 10.11 (s, 1H), 8.33 (s, 1H), 8.12 (d, J=7.8 Hz, 1H), 8.01 (d, J=7.8 Hz, 1H), 7.70 (t, J=7.8 Hz, 1H), 5.98 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 191.8 (CH), 147.3 (C), 137.2 (C), 135.4 (C), 131.5 (CH), 130.3 (CH), 129.6 (CH), 126.9 (CH), 68.1 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3203 (O−H), 1610 (C=N), 1554 and 1381 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_9H_8N_2NaO_4$ $[M+Na]^+$ 231.0382, found 231.0375.

1-(4-(Chloromethyl)phenyl)-2-nitroethanone oxime (**2k**):[9] Pale yellow solid (84.2 mg, 73% yield). m.p. 83−84 ℃ (CH_2Cl_2/hexanes); ^1H NMR (400 MHz, acetone-d_6) δ: 11.43 (s, 1H), 7.64 (d, J=8.4 Hz, 2H), 7.37 (d, J=8.4 Hz, 2H), 5.71 (s, 2H), 4.57 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 147.3 (C), 139.3 (C), 134.2 (C), 129.0 (2×CH), 126.3 (2×CH), 68.1 (CH_2), 45.4 (CH_2); IR (KBr) v: 3227 (O−H), 1605 (C=N), 1574 and 1383 (NO_2) cm^{-1}; HRMS (APCI-TOF) calcd for $C_9H_{10}ClN_2O_3$ $[M+H]^+$ 229.0380, found 229.0375.

2-Nitro-1-(*p*-tolyl)ethanone oxime (**2l**):[10d] Yellow viscous oil (77.0 mg, 79% yield). ^1H NMR (400 MHz; $CDCl_3$, isomeric ratio 18.2∶1, minor isomer marked *) δ: 9.73 (br s, 1H of major and minor isomers), 7.50 (d, J=8.0 Hz, 2H of major and minor isomers), 7.23 (d, J=8.0 Hz, 2H of major and minor isomers), 5.63 (s, 1.82H), 5.40* (s, 0.10H), 2.37 (s, 3H of major and minor isomers); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.3 (C), 140.7 (C), 130.2 (C), 129.8 (2×CH), 129.4* (2×CH), 128.3* (2×CH), 126.1 (2×CH), 78.2* (CH_2), 68.5 (CH_2), 21.5* (CH_3), 21.3 (CH_3) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) v: 3292 (O−H), 1611 (C=N), 1546 and 1377 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_9H_{10}N_2NaO_3$ $[M+Na]^+$ 217.0589, found 217.0595.

1-(4-Methoxyphenyl)-2-nitroethanone oxime (**2m**):[10d] Pale yellow solid (66.5 mg, 63% yield). m.p. 109−110 ℃ (CH_2Cl_2/hexanes); ^1H NMR (400 MHz, acetone-d_6) δ: 11.30 (s, 1H), 7.73 (dd, J=6.9, 2.0 Hz, 2H), 7.00 (dd, J=6.9, 2.0 Hz, 2H), 5.85 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz; acetone-d_6) δ: 161.0 (C), 147.4 (C), 127.5 (2×CH), 126.7 (C), 114.0 (2×CH), 68.2 (CH_2), 54.8 (CH_3); IR (KBr) v: 3229 (O−H), 1606 (C=N), 1559 and 1380 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_9H_{11}N_2O_4$ $[M + H]^+$ 211.0719, found 211.0720.

1-(4-(*tert*-Butyl)phenyl)-2-nitroethanone oxime (**2n**):[9] Yellow solid (100.7 mg, 85% yield). m.p. 102−103 ℃ (CH_2Cl_2/hexanes); ^1H NMR (400 MHz, $CDCl_3$, isomeric ratio 14.4∶1, minor isomer marked *) δ: 9.66 (br s, 1H of major and minor isomers), 7.55 (d, J=8.6 Hz, 2H of major and minor isomers), 7.45 (d, J=8.6 Hz, 2H of major and minor isomers), 5.64 (s, 1.87H), 5.41* (s, 0.13H), 1.32 (s, 9H of major and minor isomers); ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 154.0 (C), 148.5 (C), 130.0 (C), 128.2* (2×CH), 126.1 (2×CH), 126.0 (2×CH), 125.7* (2×CH), 78.1* (CH_2), 68.5 (CH_2), 34.9 (C), 31.1 (3×CH_3) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) *v*: 3300 (O−H), 1608 (C=N), 1558 and 1374 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_{12}H_{16}N_2NaO_3$ $[M+Na]^+$ 259.1059, found 259.1058.

4-(1-(Hydroxyimino)-2-nitroethyl)phenyl acetate (**2o**):[9] Yellow solid (96.6 mg, 81% yield). m.p. 114−115 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 13.3∶1, minor isomer marked *) δ: 11.61 (s, 0.80H), 11.25* (s, 0.06H), 7.83 (d, J=8.7 Hz, 2H of major and minor isomers), 7.22 (d, J=8.7 Hz, 2H of major and minor isomers), 5.89 (s, 1.86H), 5.69* (s, 0.14H), 2.28 (s, 3H of major and minor isomers); ^{13}C NMR (100 MHz, acetone-d_6) δ: 168.8 (C), 152.1 (C), 147.2 (C), 131.8 (C), 129.9* (2×CH), 127.2 (2×CH), 122.1 (2×CH), 121.7* (2×CH), 78.4* (CH_2), 68.2 (CH_2), 20.1 (CH_3) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) *v*: 3278 (O−H), 1604 (C=N), 1570 and 1369 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2NaO_5$ $[M+Na]^+$ 261.0487, found 261.0480.

2-Nitro-1-phenylethanone oxime (**2p**):[11] Yellow solid (66.3 mg, 73% yield). m.p. 95—96 ℃ (CH_2Cl_2/hexanes, lit.[11] m.p. 95 ℃); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.31 (br s, 1H), 7.63−7.61 (m, 2H), 7.46−7.41 (m, 3H), 5.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.6 (C), 132.9 (C), 130.5 (CH), 129.1 (2×CH), 126.2 (2×CH), 68.5 (CH_2); IR (KBr) *v*: 3222 (O−H), 1636 (C=N), 1559 and 1383 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_8H_8N_2NaO_3$ $[M+Na]^+$ 203.0433, found 203.0434.

2-Nitro-1-phenylpropan-1-one oxime (**2q**):[9] Yellow solid (79.1 mg, 81% yield). m.p. 96 — 97 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 2.3∶1, minor isomer marked *) δ: 11.34 (s, 0.67H), 10.91* (s, 0.30H), 7.64—7.40 (m, 5H of major and minor isomers), 6.12 (dd, J=13.7, 6.9 Hz, 0.70H), 5.84* (dd, J=13.7, 6.9 Hz, 0.30H), 1.87 (d, J=6.8 Hz, 2.00H), 1.76* (d, J=6.8 Hz, 1.00H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 152.5 (C), 151.5* (C), 134.0 (C), 131.3* (C), 129.4 (CH), 129.2* (CH), 128.6 (2×CH), 128.3* (2×CH), 128.2* (2×CH), 126.6 (2×CH), 85.4* (CH), 77.5 (CH), 16.3* (CH_3), 14.6 (CH_3); IR (KBr) *v*: 3237 (O−H), 1648 (C=N), 1546 and 1386 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_9H_{10}N_2NaO_3$ $[M+Na]^+$ 217.0589, found 217.0587.

2-Nitro-3,4-dihydronaphthalen-1(2*H*)-one oxime (**2r**):[12] Pale brown solid (67.7 mg, 70%). m.p. 138−139 ℃ (CH_2Cl_2/hexanes, lit.[12] m.p. 140−142 ℃); ^1H NMR (400 MHz, acetone-d_6) δ: 11.41 (s, 1H), 8.00 (d, J=7.7 Hz, 1H), 7.36−7.23 (m, 3H), 6.15 (dd, J=5.3, 4.2 Hz, 1H), 2.88−2.78 (m, 2H), 2.60−2.53 (m, 1H), 2.45−2.36 (m, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 146.6 (C), 137.4 (C), 129.4 (CH), 129.3 (C), 128.7 (CH), 126.8 (CH), 123.9 (CH), 77.3 (CH), 27.7 (CH_2), 24.7 (CH_2); IR (KBr) *v*: 3300 (O−H), 1598 (C=N), 1547 and 1375 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2NaO_3$ $[M+Na]^+$ 229.0589, found 229.0584.

1-(Naphthalen-1-yl)-2-nitroethanone oxime (**2s**):[9] Yellow viscous oil (69.7 mg, 60% yield); ^1H NMR (400 MHz, $CDCl_3$, isomeric ratio 1.4∶1, minor isomer marked *) δ: 9.65 (br s, 0.58H), 8.89* (br s, 0.45H), 7.97−7.83 (m, 3H of major and minor isomers), 7.64−7.33 (m, 4H of major and minor isomers), 5.59 (s, 1.16H), 5.42* (s, 0.84H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.4* (C), 149.2 (C), 133.8 (C), 133.5* (C), 130.8* (C), 130.7 (C), 130.6 (CH), 130.5* (CH), 130.3* (C), 129.4 (C), 128.8 (CH), 128.7* (CH), 127.4* (CH), 127.36 (CH), 127.1* (CH), 126.58 (CH), 126.57 (CH), 125.4* (CH), 125.20* (CH), 125.19 (CH), 125.1* (CH), 124.4 (CH), 78.9* (CH_2) , 71.6 (CH_2); IR (neat) *v*: 3273 (O−H), 1592 (C=N), 1558 and 1372 (NO_2) cm^{-1}; HRMS (ESI-TOF) calcd for $C_{12}H_{10}N_2NaO_3$ $[M+Na]^+$ 253.0589, found 253.0588.

1-(Naphthalen-2-yl)-2-nitroethanone oxime (**2t**): Yellow solid (60.1 mg, 52% yield). m.p. 115−116 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 32.3∶1, minor isomer marked *) δ: 11.67 (br s, 1H of major and minor isomers), 8.32 (d, J=0.7 Hz, 1H), 8.04−7.92 (m, 4H of major and minor isomers), 7.58−7.54 (m, 2H of major and minor isomers), 6.04 (s, 1.94H), 5.81* (s, 0.06H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 147.9 (C), 133.8 (C), 133.2 (C), 131.8 (C), 129.8* (CH), 129.5* (CH), 128.5 (CH), 128.4 (CH), 128.2* (CH), 127.9* (CH), 127.7 (CH), 127.4* (CH), 127.3* (CH), 127.0 (CH), 126.7 (CH), 126.5* (CH), 126.0 (CH), 123.1 (CH), 78.6* (CH_2) , 68.0 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) *v*: 3262 (O−H), 1625 (C=N), 1568 and 1383 (NO_2) cm^{-1}; MS *m/z* (%) relative intensity 230 (M^+, 49), 166 (100), 153 (65); HRMS (ESI-TOF) calcd for $C_{12}H_{10}N_2NaO_3$ $[M+Na]^+$ 253.0589, found 253.0590.

1-(Benzo[*b*]thiophen-2-yl)-2-nitroethanone oxime (**2u**): Yellow solid (74.8 mg, 63% yield). m.p. 152−153 ℃ (EtOAc/hexanes); ^1H NMR (400 MHz, acetone-d_6, isomeric ratio 2.9∶1, minor isomer marked *) δ: 12.19* (br s, 0.21H), 11.74 (br s, 0.65H), 8.01−7.83 (m, 3H of major and minor isomers), 7.48−7.36 (m, 2H of major and minor isomers), 5.96 (s, 1.48H), 5.89* (s, 0.52H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 144.6 (C), 139.7 (C), 139.5 (C), 138.6 (C), 126.2* (CH), 126.0 (CH), 125.8* (CH), 124.8 (CH), 124.7* (CH), 124.4 (CH), 124.3 (CH), 122.2 (CH), 121.9* (CH), 77.3* (CH_2), 67.7 (CH_2) (Some peaks of the minor isomer could not be detected by ^{13}C NMR due to their low intensity); IR (KBr) *v*: 3255 (O−H), 1623 (C=N), 1560 and 1381 (NO_2) cm^{-1}; MS *m/z* (%) relative intensity 236 (M^+, 21), 172 (16), 147 (100); HRMS (ESI-TOF) calcd for $C_{10}H_8N_2NaO_3S$ $[M+Na]^+$ 259.0153, found 259.0152.

1-(Benzofuran-2-yl)-2-nitroethanone oxime (**2v**):

Yellow solid (84.2 mg, 77% yield). m.p. 124－125 ℃ (EtOAc/hexanes); ^{1}H NMR (400 MHz, acetone-d_6, isomeric ratio 0.6∶1, minor isomer marked *) δ: 12.11 (br s, 1H of major and minor isomers), 7.97 (s, 1H of major and minor isomers), 7.79 (d, J=7.8 Hz, 0.6H), 7.70* (d, J=7.8 Hz, 0.4H), 7.58－7.55 (m, 1H of major and minor isomers), 7.47－7.39 (m, 1H of major and minor isomers), 7.35－7.28 (m, 1H of major and minor isomers), 5.89* (s, 0.77H), 5.79 (s, 1.23H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 155.2* (C), 153.2 (C), 150.6* (C), 145.2 (C), 140.9* (C), 138.9 (C), 128.3 (C), 128.1* (C), 126.8 (CH), 126.0* (CH), 123.7 (CH), 123.5* (CH), 122.6 (CH), 121.8* (CH), 113.9 (CH), 111.4 (CH), 111.3* (CH), 106.9* (CH), 75.2 (CH_2), 67.5* (CH_2); IR (KBr) v: 3286 (O－H), 1611 (C＝N), 1563 and 1375 (NO_2) cm^{-1}; MS m/z (%) relative intensity 220 (M^+, 14), 131 (100), 115 (46); HRMS (ESI-TOF) calcd for $C_{10}H_8N_2NaO_4$ $[M+Na]^+$ 243.0382, found 243.0384.

(3*E*)-1-Nitro-4-phenylbut-3-en-2-one oxime (**2w**): Orange solid (27.1 mg, 25% yield). m.p. 125－126 ℃ (EtOAc/hexanes); ^{1}H NMR (400 MHz, acetone-d_6, isomeric ratio 1∶1) δ: 11.41 (br s, 0.40H), 11.28 (br s, 0.46H), 7.64－7.57 (m, 2.31H), 7.45－7.32 (m, 3H) 7.23 (dd, J=16.7, 10.8 Hz, 1H), 7.03 (d, J=16.7 Hz, 0.45H), 5.75 (s, 0.94H), 5.62 (s, 1.06H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 148.7 (C), 147.3 (C), 136.3 (C), 136.0 (C), 135.7 (C), 133.5 (C), 129.3 (CH), 128.9 (2×CH), 128.8 (2×CH), 128.6 (CH), 127.4 (2×CH), 126.9 (2×CH), 123.7 (CH), 114.7 (CH), 75.3 (CH_2), 66.3 (CH_2); IR (KBr) v: 3237 (O－H), 1625 (C＝N), 1556 and 1373 (NO_2) cm^{-1}; MS m/z (%) relative intensity 206 (M^+, 6), 160 (58), 115 (100); HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2NaO_5$ $[M+Na]^+$ 229.0589, found 229.0586.

(3*E*)-4-(Benzo[*d*][1,3]dioxol-5-yl)-1-nitrobut-3-en-2-one oxime (**2x**): Yellow liquid (12.2 mg, 28% yield). ^{1}H NMR (400 MHz, acetone-d_6, isomeric ratio 1∶1) δ: 11.26 (br s, 0.40H), 11.13 (br s, 0.50H), 7.40 (d, J=16.8 Hz, 0.58H), 7.21－7.02 (m, 3H), 6.86 (t, J=8.2 Hz, 1.48H), 6.05 (s, 1.20H), 6.04 (s, 0.81H), 5.70 (s, 0.88H), 5.57 (s, 1.12H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 148.7 (C), 147.4 (C), 135.5 (CH), 133.3 (CH), 130.8 (C), 130.5 (C), 123.4 (CH), 122.6 (CH), 121.9 (CH), 113.0 (CH), 108.4 (CH), 108.3 (CH), 105.8 (CH), 105.5 (CH), 101.7 (CH_2), 101.5 (CH_2), 75.3 (CH_2), 66.3 (CH_2); IR (KBr) v: 3256 (O－H), 1624 (C＝N), 1559 and 1376 (NO_2), 1257 (C－O) cm^{-1}; MS m/z (%) relative intensity 250 (M^+, 48), 204 (41), 187 (100); HRMS (ESI-TOF) calcd for $C_{11}H_{10}N_2NaO_5$ $[M+Na]^+$ 273.0487, found 273.0489.

(3*E*)-4-(2-Methoxyphenyl)-1-nitrobut-3-en-2-one oxime (**2y**): Orange liquid (19.1 mg, 13% yield); ^{1}H NMR (400 MHz, acetone-d_6, isomeric ratio 1∶1) δ: 11.33 (br s, 0.38H), 11.19 (br s, 0.47H), 7.67－7.59 (m, 1.52H), 7.44－7.31 (m, 2H) 7.09－6.97 (m, 2.46H), 5.75 (s, 0.89H), 5.61 (s, 1.11H), 3.90 and 3.97 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 157.8 (C), 157.4 (C), 149.1 (C), 147.8 (C), 130.7 (CH), 130.4 (CH), 129.9 (CH), 128.4 (CH), 127.4 (CH), 127.2 (CH), 124.8 (C), 124.5 (C), 124.1 (CH), 120.8 (CH), 120.7 (CH), 115.0 (CH), 111.4 (CH), 111.3 (CH), 75.5 (CH_2), 66.4 (CH_2), 55.2 (CH_3), 55.1 (CH_3); IR (KBr) v: 3276 (O－H), 1618 (C＝N), 1560 and 1341 (NO_2), 1249 (C－O) cm^{-1}; MS m/z (%) relative intensity 236 (M^+, 1), 205 (55), 159 (100); HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2NaO_5$ $[M+Na]^+$ 259.0695, found 259.0690.

General procedure for oxidative hydrolysis of α-nitrooximes 2

To a solution of α-nitrooxime **2** (0.5 mmol) in CH_2Cl_2 (2 mL), $NaNO_2$ (34.5 mg, 0.5 mmol), Amberlyst®-15 (157.2 mg, 0.5 mmol) and H_2O (1 mL) were added at 0－5 ℃. The resulting mixture was slowly warmed to room temperature (32－35 ℃). After 2 h, the Amberlyst®-15 was filtered off and washed with CH_2Cl_2. The filtrate was extracted with CH_2Cl_2 (10 mL ×3). The combined CH_2Cl_2 extracts were washed with H_2O (10 mL), brine (10 mL), dried (anhydrous $MgSO_4$), filtered and vacuumed (aspirator). The crude residue was purified by column chromatography (SiO_2) using EtOAc/hexanes as eluent to provide the corresponding α-nitroketone product.

1-(4-Bromophenyl)-2-nitroethanone (**4a**):[13] White solid (97.4 mg, 80% yield). m.p. 139－140 ℃ (EtOAc/hexanes, lit.[13] m.p. 142－143 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77－7.69 (m, 4H), 5.85 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.7 (C), 136.8 (C), 132.8 (2×CH), 129.6 (2×CH), 128.2 (C), 81.0 (CH_2).

1-(4-(Chloromethyl)phenyl)-2-nitroethanone (**4k**): Pale yellow solid (92.3 mg, 87% yield). m.p. 126－127 ℃ (EtOAc/hexanes); ^{1}H NMR (400 MHz, acetone-d_6) δ: 8.05 (d, J=8.3 Hz, 2H), 7.71 (d, J=8.3 Hz, 2H), 6.41 (s, 2H), 4.84 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ: 187.1 (C), 144.7 (C), 133.6 (C), 129.3 (2×CH), 128.8 (2×CH), 82.2 (CH_2), 44.8 (CH_2); IR (KBr) v: 3031 (ArH), 1699 (C＝O), 1560 and 1387 (NO_2) cm^{-1}; MS m/z (%) relative intensity 213 (M^+, 2), 178 (100), 161 (46); HRMS (ESI-TOF) calcd for $C_9H_8ClNO_3$ $[M+Na]^+$ 236.0090, found 236.0081.

2-Nitro-1-(*p*-tolyl)ethanone **(4l)**:[13] White solid (69.9 mg, 77% yield). m.p. 137－138 ℃ (EtOAc/hexanes, lit.[13] m.p. 139－140 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, J=8.2 Hz, 2H), 7.34 (d, J=8.2 Hz, 2H), 5.88 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.3 (C), 146.5 (C), 135.9 (C), 130.0 (2×CH), 128.4 (2×CH), 81.3 (CH_2), 21.9 (CH_3).

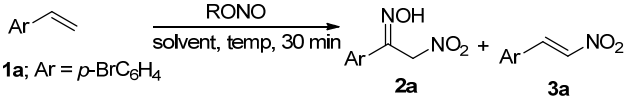
2-Nitro-1-phenylethanone **(4p)**:[13] Pale yellow solid (70.2 mg, 85% yield). m.p. 101－102 ℃ (EtOAc/hexanes, lit.[13] m.p. 103－105 ℃); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.88 (d, J=7.8 Hz, 2H), 7.70 (t, J=7.4 Hz, 1H), 7.55 (t, J=7.8 Hz, 2H), 5.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.9 (C), 135.4 (CH), 129.3 (2×CH), 128.3 (2×CH), 126.9 (C), 81.4 (CH_2).

Results and Discussion

The generation of NO radical from *tert*-butyl nitrite

(*t*-BuONO) and its conversion to the NO_2 radical under aerobic conditions has been well precedent in the literature.[14] Thus, we envisaged that *tert*-butyl nitrite, a safe and easily handled non-metallic reagent capable of generating a NO radical, would trigger a one-pot nitration-oximization of olefins. In a preliminary set of experiments employing 4-bromostyrene as a benchmark substrate with *t*-BuONO in different solvents confirmed the validity of our hypothesis, as the corresponding *α*-nitrooxime derived from 4-bromostyrene was obtained in variable yields depending on type of solvents (Table 1). In the initial experiment, 4-bromostyrene was allowed to react with *t*-BuONO (2 equiv.) in CH_2Cl_2 at room temperature (32—35 ℃) for 30 min leading to poor yields of *α*-nitrooxime **2a** (9% yield) and nitroalkene **3a** (*E* isomer, 3% yields) (Table 1, Entry 1). The reactions did not proceed when acetone and methanol (MeOH) were employed as the solvents; the 4-bromostyrene was untouched (TLC analysis) (Table 1, Entries 2—3). Nitroalkene **3a** was obtained as a sole product when ethyl acetate (EtOAc) was employed as the solvent (Table 1, Entry 4). The reactions performed in tetrahydrofuran (THF), acetonitrile (CH_3CN), *N*,*N*-dimethylformamide (DMF) and water (H_2O) led to significant improvement; **2a** was isolated in moderate yields along with the formation of nitroolefin **3a** in all cases (Table 1, Entries 5—8). It is worth also to mention here that except DMSO where **2a** was isolated as a single isomer, all other solvents attempted in Table 1 yielded **2a** as a mixture of two isomers.[9,15] The *Z* isomer whose methylnitro group is *syn* to the hydroxy group being stabilized through the hydrogen bonding was believed to be formed as a major isomer. In comparison with a closely related structure, the ^{1}H NMR signals of the methylene protons of the *Z* isomer resonate at a lower field than those of the *E* isomer due to the deshielding effect of the electronegative oxygen atom.[15] On this basis, the ratios of the *E* and *Z* isomers of *α*-nitrooximes **2** could be assigned. Gratifyingly, the use of dimethyl sulfoxide (DMSO) as the solvent led to the best yield of **2a** (87% yield) along with **3a** (7% yield) (Table 1, Entry 9). An increase in the stoichiometry of *t*-BuONO (from 2 equiv. to 3 equiv.) was found harmful to the reaction efficiency; unidentifiable mixtures were observed (baseline, TLC analysis) (Table 1, Entry 10). Prolonged reaction time and an increasing reaction temperature (from r.t. to 100 ℃) did not help to improve the results (Table 1, Entries 11—12). When *t*-BuONO was replaced by isoamyl nitrite (*i*-AmONO), **2a** was isolated in poorer yield (45% yield) (Table 1, Entry 13). Finally, the reaction performed in degassed DMSO and under an Ar atmosphere proved to be less efficient; **2a** was obtained in lower yield (37% yield) (Table 1, Entry 14). From the results shown in Table 1, the optimum reaction conditions could be identified and are to treat the substrate with *t*-BuONO (2 equiv.) in DMSO at room temperature for 30 min (Table 1, Entry 9).

Table 1 Solvent and reagent optimization[a]



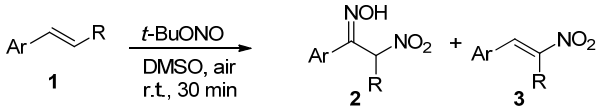
Entry	RONO	Solvent	Yield[b]/%	
			2a[c]	**3a**
1	*t*-BuONO	CH_2Cl_2	9	3
2	*t*-BuONO	Acetone	—	—
3	*t*-BuONO	MeOH	—	—
4	*t*-BuONO	EtOAc	—	30
5	*t*-BuONO	THF	64	9
6	*t*-BuONO	CH_3CN	44	12
7	*t*-BuONO	DMF	36	10
8	*t*-BuONO	H_2O	36	18
9	***t*-BuONO**	**DMSO**	**87**	**7**
10	*t*-BuONO[d]	DMSO	25	0
11[e]	*t*-BuONO	DMSO	75	14
12[f]	*t*-BuONO	DMSO	79	4
13	*i*-AmONO	DMSO	45	5
14[g]	*t*-BuONO	DMSO	37	—

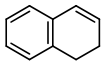
[a] Reaction conditions: **1** (0.5 mmol) and RONO (2 equiv.) in solvent (2.5 mL) under an air atmosphere at room temperature (32—35 ℃) for 30 min. [b] Isolated yield. [c] Except DMSO, all other solvents yielded **2a** as a mixture of two isomers (*E* (minor) and *Z* (major)). [d] *t*-BuONO (3 equiv.) was employed. [e] Reaction time: 60 min. [f] The reaction was performed at 100 ℃. [g] Employing degassed DMSO and under an Ar atmosphere.

After having the optimized conditions in hands, transformation of a collection of styrene substrates was examined and the results were summarized in Table 2. In most cases, the *α*-nitrooximes **2** were obtained as a mixture of two isomers as evidenced by ^{1}H NMR analysis of the crude mixtures and analytically pure products after chromatographic purification and in most cases the corresponding nitroalkenes **3** were isolated in variable yields. Notably, the nitration-oximization reactions employing *t*-BuONO in DMSO was superior to those employing $NaNO_2$/OXONE® in aqueous acetonitrile[9] in that the crude mixture was cleaner (TLC analysis) and the *α*-nitrooxime products were easily isolated. Halogen-substituted styrene derivatives yielded their corresponding *α*-nitrooximes in moderate to good yields (60%—87% yields) (Table 2, Entries 1—6). Styrene derivatives bearing electron-withdrawing substituents including NO_2 and CO_2Me groups and sensitive substituents including —CHO and —CH_2Cl groups readily underwent the reaction to give the corresponding products in moderate yields (60%—73% yields, Table 2, Entries 7—11). While a combination of $NaNO_2$/OXONE® in aqueous acetonitrile was found less efficient, the use of *t*-BuONO in DMSO was found to be well accommodated with electron-donating substituted derivatives including 4-Me-, 4-MeO- and 4-*t*-Bu-sub-

stituted styrenes; the corresponding products were obtained in high yields (63%—85% yield) (Table 2, Entries 12—14). Significantly improved yields (60%—81% yields) were also observed with the reactions of 4-acetoxystyrene, a simple styrene, *β*-methylstyrene, 1,2-dihydronaphthalene and 1-vinylnaphthalene (Table 2, Entries 15—19). While $NaNO_2$/OXONE® in aqueous acetonitrile led to complex and unidentifiable mixtures, the reaction of 2-vinylnaphthalene with *t*-BuONO under the standard reaction conditions provided *α*-nitrooxime **2t** in 52% yield (Table 2, Entry 20). It is worth to note that scaling up experiments (10 mmol scale) for the reactions of 4-bromostyrene and styrene were also investigated under the optimized conditions (Scheme 2). *α*-Nitrooximes **2a** and **2p** were obtained in similar efficiency in 82% and 72% yields, respectively.

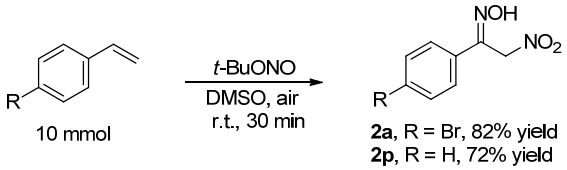
Table 2 Nitration-oximization reaction of styrene derivatives[a]



Entry	Substrate		Product; yield[b]/%	
	Ar	R	**2** (isomer ratio)[c]	**3**
1	4-BrC_6H_4	H	**2a**; 87 (single isomer)	**3a**; 7
2	4-ClC_6H_4	H	**2b**; 74 (single isomer)	**3b**; 6
3	3-ClC_6H_4	H	**2c**; 74 (13.3∶1)	**3c**; 8
4	2-ClC_6H_4	H	**2d**; 60 (1.6∶1)	**3d**; 8
5	4-FC_6H_4	H	**2e**; 71 (8.5∶1)	**3e**; 8
6	3-FC_6H_4	H	**2f**; 74 (26.9∶1)	**3f**; 5
7	4-$NO_2C_6H_4$	H	**2g**; 62 (21.2∶1)	**3g**; 7
8	3-$NO_2C_6H_4$	H	**2h**; 66 (20.6∶1)	**3h**; 9
9	4-(MeO_2C)C_6H_4	H	**2i**; 60 (27.6∶1)	**3i**; 0
10	3-$OHCC_6H_4$	H	**2j**; 66 (single isomer)	**3j**; 6
11	4-($ClCH_2$)C_6H_4	H	**2k**; 73 (single isomer)	**3k**; 4
12	4-MeC_6H_4	H	**2l**; 79 (18.2∶1)	**3l**; 5
13	4-$MeOC_6H_4$	H	**2m**; 63 (single isomer)	**3m**; 5
14	4-*t*-BuC_6H_4	H	**2n**; 85 (14.4∶1)	**3n**; 3
15	4-$AcOC_6H_4$	H	**2o**; 81 (13.3∶1)	**3o**; 3
16	C_6H_5	H	**2p**; 73 (single isomer)	**3p**; 7
17	C_6H_5	CH_3	**2q**; 81 (2.3∶1)	**3q**; 6
18		H	**2r**; 70 (single isomer)[d]	**3r**; 0
19	1-Naphthyl	H	**2s**; 60 (1.4∶1)	**3s**; 3
20	2-Naphthyl	H	**2t**; 52 (32.3∶1)	**3t**; 0

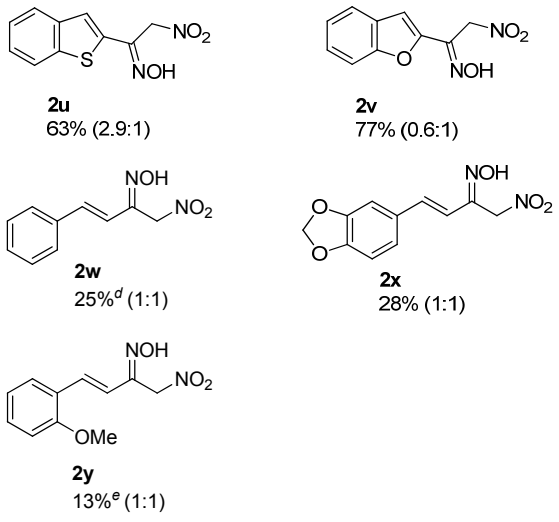
[a] Reaction conditions: **1** (0.5 mmol) and *t*-BuONO (2 equiv.) in DMSO (2.5 mL), under an air atmosphere at room temperature (32—35 ℃) for 30 min. [b] Isolated yield; in most cases their corresponding nitroalkenes (*E* isomers) were isolated in the range of 3%—9% yields. [c] The isomeric ratio (*Z*∶*E* ratio) was determined by ^{1}H NMR analysis. [d] ^{1}H NMR spectrum of the crude mixture exhibited a mixture of two isomers in a ratio of 10∶1.

Scheme 2 Scaling up reactions of 4-bromostyrene and styrene



Having demonstrated the synthetic utilities of the present protocol to a collection of styrene derivatives bearing electronically different substituents, the reactions of vinyl-substituted heteroaromatic compounds, aliphatic alkenes, electron deficient alkenes (*α*,*β*-unsaturated ester) and 1-aryl-1,3-butadienes were also evaluated. The results are summarized in Table 3. 2-Vinylbenzothiophene and 2-vinylbenzofuran also gave the corresponding products in 63% and 77% yields, respectively (Table 3). Unfortunately, aliphatic alkenes (1-octene and cyclohexene), 2- and 3-vinylpyridines and *n*-butyl acrylate failed to provide the desired products; only starting compounds were observed (^{1}H NMR analysis). Finally, the reactions of 1-aryl-1,3-butadienes selectively led to products **2w**—**2y** derived from a 1,2-addition at the terminal carbon of 1-aryl-1,3-butadienes in low yields (13%—28% yields). Attempts to improve the yield of **2w** by performing the reaction at prolonged reaction time (from 30 min. to 2 h), at higher temperature (from r.t. to 100 ℃), or by increasing the stoichiometry of *t*-BuONO (from 2 equiv. to 3 equiv.) led to inferior results; extensive decomposition was observed (TLC analysis).

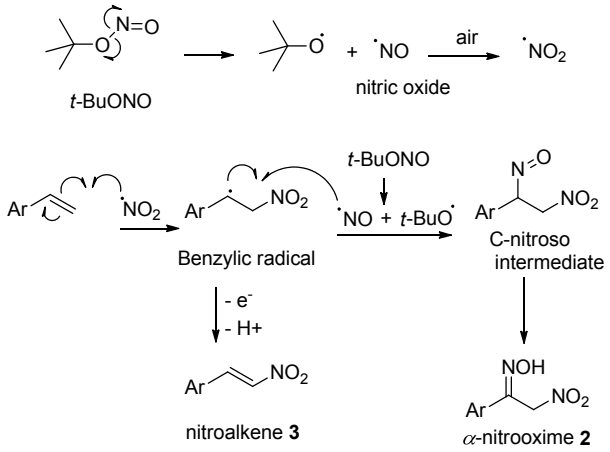
Table 3 Nitration-oximization reaction of 2-vinylbenzothiophene, 2-vinylbenzofuran and 1-aryl-1,3-butadienes[a,b,c]



[a] Reaction conditions: Substrate (0.5 mmol) and *t*-BuONO (2 equiv.) in DMSO (2.5 mL) under an air atmosphere at room temperature (32—35 ℃) for 30 min. [b] Isolated yield. [c] The isomeric ratio (*Z*∶*E* ratio)was determined by ^{1}H NMR analysis. [d] Starting materials underwent decomposition under the reaction conditions and could not be recovered. [e] The starting diene was recovered (60% yield).

On the basis of the precedent literature, we suggested that the present transformation proceeded through a pathway involving the NO/NO_2 radicals. To validate the radical mechanism, the reaction of 4-bromostyrene under the standard reaction conditions was carried out in the presence of radical scavengers. Addition of TEMPO (1 equiv.) or BHT (1 equiv.) ceased the reaction. Additionally, oxygen or air was found crucial for the reaction to proceed since the reaction performed in degassed DMSO and purged with Ar gas gave poor result (Table 1, Entry 14). A plausible mechanism of this one-pot nitration-oximization of styrene derivatives is shown in Scheme 3. A homolytic cleavage of the *t*-BuONO occurs to generate *tert*-butoxy radical and nitric oxide (NO) followed by the conversion of NO to NO_2 radical under aerobic conditions.[10e,14d-14g,16] Subsequently, the generated NO_2 radical attacks styrene derivatives to generate a more stable benzylic radical. Under high concentration of *t*-BuONO, the benzylic radical can be rapidly trapped with another molecule of NO generating *C*-nitroso derivative which readily undergoes tautomerization, leading to the observed α-nitrooximes **2** which in most cases were obtained as a mixture of two isomers (*E* and *Z*). Alternatively, the benzylic radical can be oxidized followed by deprotonation, yielding nitroalkenes **3** (*E* isomer).

Scheme 3 Plausible reaction mechanism

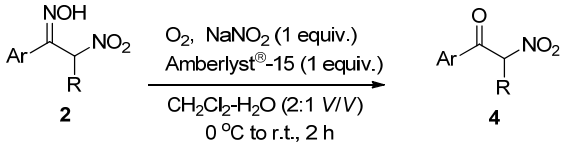


α-Nitrooxime compounds are synthetically useful motifs in organic synthesis.[17] In this work, some of the prepared α-nitrooxime compounds were readily converted to α-nitroketones. Several reaction conditions were attempted to convert an oxime moiety to the corresponding keto group.[18] Gratifyingly, upon treatment of α-nitrooximes **2** with $NaNO_2$, Amberlyst®-15 under O_2 atmosphere, the respective α-nitroketones **4** were obtained in good yields (77%—85% yields). The results are summarized in Table 4.

Conclusions

In summary, we have developed a practical and efficient nitration-oximization of styrene derivatives using *tert*-butyl nitrite in DMSO at room temperature. The present work is superior to the previously reported methods[10,14] as follows: (i) metal-free reagent, (ii) mild reaction conditions, (iii) environmentally benign solvent and (iv) simple experimental procedure and safe. Therefore, the present protocol offers a general and practical method for the synthesis of α-nitrooxime compounds, although limited to those derived from styrene derivatives. Additionally, the reaction can be scaled up to 10 mmol scale and the prepared α-nitrooximes can be readily converted to α-nitroketones in good yields.

Table 4 Hydrolysis of α-nitrooxime[a]



Entry	Substrate		Product; yield[b]/%
	Ar	R	**4**
1	4-BrC_6H_4	H	**4a**; 80
2	4-$(ClCH_2)C_6H_4$	H	**4k**; 87
3	4-MeC_6H_4	H	**4l**; 77
4	C_6H_5	H	**4p**; 85

[a] Reaction conditions: **2** (0.5 mmol), $NaNO_2$ (1 equiv.) and Amberlyst®-15 (1 equiv.) in CH_2Cl_2/H_2O (2∶1 mL) were stirred at 0 ℃ to room temperature (32—35 ℃) for 2 h. [b] Isolated yield.

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References

[1] (a) Anastas, P. T.; Kirchhoff, M. M. *Acc. Chem. Res.* **2002**, *35*, 686; (b) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695.

[2] (a) Mizuno, N.; Misono, M. *Chem. Rev.* **1998**, *98*, 199; (b) Akiyama, R.; Kobayashi, S. *Chem. Rev.* **2009**, *109*, 594; (c) Ikegami, S.; Hamamoto, H. *Chem. Rev.* **2009**, *109*, 583; (d) Climent, M.; Corma, J. A.; Iborra, S. *Chem. Rev.* **2011**, *111*, 1072; (e) Guo, Z.; Liu, B.; Zhang, Q.-H.; Deng, W.-P.; Wang, Y.; Yang, Y.-H. *Chem. Soc. Rev.* **2014**, *43*, 3480; (f) Zhang, Y.; Cui, X.-J.; Shi, F.; Deng, Y.-Q. *Chem. Rev.* **2012**, *112*, 2467.

[3] (a) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996; (b) Xu, K.; Hu, Y.-B.; Zhang, S.; Zha, Z.-G.; Wang, Z.-Y. *Chem. Eur. J.* **2012**, *18*, 9793; (c) Arancon, R. A. D.; Lin, C. S. K.; Vargas, C.; Luque, R. *Org. Biomol. Chem.* **2014**, *12*, 10.

[4] (a) Rao, C. B.; Chinnababu, B.; Venkateswarlu, Y. *J. Org. Chem.*

2009, *74*, 8856; (b) Zhou, L.; Tan, C.-K.; Zhou, J.; Yeung, Y.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 10245; (c) Kumar, A.; Kumar, M.; Gupta, M. K. *Green Chem.* **2012**, *14*, 2677; (d) Gawande, M. B.; Bonifácio, V. D. B.; Luque, R.; Brancoa, P. S.; Varma, R. S. *Chem. Soc. Rev.* **2013**, *42*, 5522; (e) Yang, Y.; Tang, L.; Zhang, S.; Guo, X.; Zha, Z.; Wang, Z. *Green Chem.* **2014**, *16*, 4106.

[5] For reviews on 1,2-diamines, see: (a) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161; (b) Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem.*, *Int. Ed.* **1998**, *37*, 2580; (c) Viso, A.; de la Pradilla, R. F.; García, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167; (d) Bogatcheva, E.; Hanrahan, C.; Nikonenko, B.; Samala, R.; Chen, P.; Gearhart, J.; Barbosa, F.; Einck, L.; Nacy, C. A.; Protopopova, M. *J. Med. Chem.* **2006**, *49*, 3045; (e) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101; (f) Kizirian, J.-C. *Chem. Rev.* **2008**, *108*, 140; (g) Grygorenko, O. O.; Radchenko, D. S.; Volochnyuk, D. M.; Tolmachev, A. A.; Komarov, I. V. *Chem. Rev.* **2011**, *111*, 5506.

[6] (a) Okada, A.; Shibuguchi, T.; Ohshima, T.; Masu, H.; Yamaguchi, K.; Shibasaki, M. *Angew. Chem.*, *Int. Ed.* **2005**, *44*, 4564; (b) Uraguchi, D.; Koshimoto, K.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 10878; (c) Handa, S.; Gnanadesikan, V.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 4925; (d) Davis, T. A.; Johnston, J. N. *Chem. Sci.* **2011**, *2*, 1076; (e) Olson, D. E.; Roberts, D. A.; Bois, J. D. *Org. Lett.* **2012**, *14*, 6174; (f) Kano, T.; Sakamoto, R.; Akakura, M.; Maruoka, K. *J. Am. Chem. Soc.* **2012**, *134*, 7516; (g) Liew, S. K.; He, Z.; St Denis, J. D.; Yudin, A. K. *J. Org. Chem.* **2013**, *78*, 11637; (h) Noble, A.; Anderson, J. C. *Chem. Rev.* **2013**, *113*, 2887.

[7] (a) de Figueiredo, R. M. *Angew. Chem.*, *Int. Ed.* **2009**, *48*, 1190; (b) Ramirez, T. A.; Zhao, B.; Shi, Y. *Chem. Soc. Rev.* **2012**, *41*, 931; (c) Muñiz, K.; Martínez, C. *J. Org. Chem.* **2013**, *78*, 2168; (d) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308; (e) Zhao, B.; Peng, X.; Zhu, Y.; Ramirez, T. A.; Cornwall, R. G.; Shi, Y. *J. Am. Chem. Soc.* **2011**, *133*, 20890; (f) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem.*, *Int. Ed.* **2011**, *50*, 9478; (g) Kim, H. J.; Cho, S. H.; Chang, S. *Org. Lett.* **2012**, *14*, 1424; (h) Ingalls, E. L.; Sibbald, P. A.; Kaminsky, W.; Michael, F. E. *J. Am. Chem. Soc.* **2013**, *135*, 8854; (i) Cornwall, R. G.; Zhao, B.; Shi, Y. *Org. Lett.* **2013**, *15*, 796; (j) Turnpenny, B. W.; Chemler, S. R. *Chem. Sci.* **2014**, *5*, 1786; (k) Zhang, B.; Studer, A. *Org. Lett.* **2014**, *16*, 1790.

[8] (a) Katrun, P.; Chiampanichayakul, S.; Korworapan, K.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T.; Kuhakarn, C. *Eur. J. Org. Chem.* **2010**, 5633; (b) Samakkanad, N.; Katrun, P.; Techajaroonjit, T.; Hlekhlai, S.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T.; Soorukram, D.; Kuhakarn, C. *Synthesis* **2012**, *44*, 1693; (c) Muangkaew, C.; Katrun, P.; Kanchanarugee, P.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Jaipetch, T.; Kuhakarn, C. *Tetrahedron* **2013**, *69*, 8847; (d) Hlekhlai, S.; Samakkanad, N.; Sawangphon, T.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Jaipetch, T.; Kuhakarn, C. *Eur. J. Org. Chem.* **2014**, 7433.

[9] Chumnanvej, N.; Samakkanad, N.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T.; Soorukram, D.; Kuhakarn, C. *RSC Adv.* **2014**, *4*, 59726.

[10] (a) Scheinbaum, M. L. *J. Org. Chem.* **1970**, *35*, 2790; (b) Uppu, R. M.; Pryor, W. A. *Anal. Biochem.* **1996**, *236*, 242; (c) Grossi, L.; Montevecchi, P. C.; Strazzari, S. *Eur. J. Org. Chem.* **2001**, 741; (d) Shaabani, A.; Bijanzadeh, H. R.; Karimi, A. R.; Teimouri, M. B.; Soleimani, K. *Can. J. Chem.* **2008**, *86*, 248; (e) Cao, Q.; Liu, J.; Yu, L.; Gui, Q.; Chen, X.; Tan, Z. *Synth. Commun.* **2015**, *45*, 2181.

[11] Duranti, E.; Balsamini, C.; Spadoni, G.; Lamberto, S. *J. Org. Chem.* **1988**, *53*, 2870.

[12] Kametani, T.; Sugahara, H.; Yagi, H. *J. Chem. Soc. C* **1966**, *7*, 717.

[13] Takamoto, M.; Kurouchi, H.; Otani, Y.; Ohwada, T. *Synthesis* **2009**, 4129.

[14] (a) Koley, D.; Colon, O. C.; Savinov, S. N. *Org. Lett.* **2009**, *11*, 4172; (b) Galliker, B.; Kissner, R.; Nauser, T.; Koppenol, W. H. *Chem. Eur. J.* **2009**, *15*, 6161; (c) Wu, X. F.; Schranck, J.; Neumann, H.; Beller, M. *Chem. Commun.* **2011**, *47*, 12462; (d) Taniguchi, T.; Yajima, A.; Ishibashi, H. *Adv. Synth. Catal.* **2011**, *353*, 2643; (e) Taniguchi, T.; Sugiura, Y.; Hatta, T.; Yajima, A.; Ishibashi, H. *Chem. Commun.* **2013**, *49*, 2198; (f) Kilpatrick, B.; Heller, M.; Arns, S. *Chem. Commun.* **2013**, *49*, 514; (g) Maity, S.; Naveen, T.; Sharma, U.; Maiti, D. *Org. Lett.* **2013**, *15*, 3384; (h) Manna, S.; Jana, S.; Saboo, T.; Maji, A.; Maiti, D. *Chem. Commun.* **2013**, *49*, 5286; (i) Rokade, B. V.; Prabhu, K. R. *Org. Biomol. Chem.* **2013**, *11*, 6713; (j) Shen, T.; Yuan, Y.; Jiao, N. *Chem. Commun.* **2014**, *50*, 554; (k) Dutta, U.; Maity, S.; Kancherla, R.; Maiti, D. *Org. Lett.* **2014**, *16*, 6302; (l) Hao, X.-H.; Gao, P.; Song, X.-R.; Qiu, Y.-F.; Jin, D.-P.; Liu, X.-Y.; Liang, Y.-M. *Chem. Commun.* **2015**, *51*, 6839.

[15] (a) Baji, H.; Flammang, M.; Kimny, T.; Gasquez, F.; Compagnon, P. L.; Delcourt, A. *Eur. J. Med. Chem.***1995**, *30*, 617; (b) Balsamo, A.; Breschi, M. C.; Chiellini, G.; Favero, L.; Macchia, M.; Martinelli, A.; Martini, C.; Rossello, A.; Scatizzi, R. *Eur. J. Med. Chem.* **1995**, *30*, 743; (c) Karakurt, A.; Alagöz, M. A.; Sayoğlu, B.; Çaliş, Ü.; Dalkara, S. *Eur. J. Med. Chem.* **2012**, *57*, 275.

[16] (a) Grossi, L. *Chem. Eur. J.* **2005**, *11*, 5419; (b) He, X.; Shen, Z.; Mo, W.; Sun, N.; Hu, B.; Hu, X. *Adv. Synth. Catal.* **2009**, *351*, 89; (c) Galliker, B.; Kissner, R.; Nauser, T.; Koppenol, W. H. *Chem. Eur. J.* **2009**, *15*, 6161.

[17] (a) Curini, M.; Epifano, F.; Carla, M.; Rosati, O.; Ballini, R.; Bosica, G. *Tetrahedron Lett.* **2000**, *41*, 8817; (b) Ovchinnikov, I. V.; Finogenov, A. O.; Epishina, M. A.; Kulikov, A. S.; Strelenko, Yu. A.; Makhova, N. N. *Russian Chem. Bull.* **2009**, *58*, 2137; (c) Zhao, J.-Q.; Zhou, M.-Q.; Zuo, J.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *Tetrahedron* **2015**, *71*, 1560.

[18] (a) Krishnaveni, N. S.; Surendra, K.; Nageswar, Y. V. D.; Rao, K. R. *Synthesis* **2003**, 1968; (b) Ganguly, N. C.; Nayek, S.; Barik, S. K. *Synth. Commun.* **2009**, *39*, 4053; (c) Quan, N.; Shi, X.-X.; Nie, L.-D.; Dong, J.; Zhu, R.-H. *Synlett* **2011**, 1028.

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