Photochemistry of 2-Nitrobenzyl Enol Ethers: Oxidative C=C Bond Scission

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Supporting information

EXPERIMENTAL

General

All solvents were distilled before use. Commercially available reagents, obtained from Acros Organics were used as received. LiHMDS (23% in methyl *tert*-butyl ether) as purchased. Reactions were monitored by thin-layer chromatography (TLC) and visualization was accomplished with a UV lamp. Reaction mixtures were purified by column chromatography, performed with the indicated solvents using silica gel (230–400 mesh). The R_f values were calculated based on the eluents used for purification. The yields reported refer to chromatographically and spectroscopically pure compounds except for the photolysis yields that were obtained by GC/MS analysis (HP 5890 Series II GC fitted with HP 5971 Series Mass Selective Detector). The photolysis experiments were performed using a Rayonet photochemical reactor. ^1H and proton decoupled ^{13}C NMR spectra were recorded on a Bruker AMX 500 MHz spectrometer at ambient temperature.

Synthesis

***o*-Nitrobenzyl methylthiomethyl ether (2).** A solution of 2-nitrobenzyl alcohol (0.332 g, 2.168 mmols) in 20 mL of DMSO was treated with 15 mL of acetic anhydride and 10 mL of acetic acid

and was allowed to stir for 27 h at room temperature. The resulting mixture was added dropwise to 50 mL of saturated NaHCO_3 and stirred for 24 h. The organic layer was extracted four times with 100 mL mixture of hexanes-ethyl acetate (1:1), dried with anhydrous magnesium sulfate and the solvent was then evaporated under reduced pressure. The residue was purified on a column of silica gel (240–400 mesh) eluting with hexanes-ethyl acetate (70:30). Yield = 0.228 g (50%) from 0.332 g nitrobenzyl alcohol, yellowish brown liquid, $R_f = 0.68$; ^1H NMR (CDCl_3) δ : 8.10 (dd, $J_1 = 1.2$ Hz, $J_2 = 8.2$, 1H), 7.80 (dd, $J_1 = 0.7$, $J_2 = 7.8$, 1H), 7.70 (t, 1H), 7.50 (t, 1H), 5.00 (s, 2H), 4.80 (s, 2H), 2.20 (s, 3H); ^{13}C NMR (CDCl_3) δ : 147.9, 134.7, 134.0, 129.3, 128.5, 125.1, 75.9, 67.0, 14.6.

***o*-Nitrobenzyl chloromethyl ether (3).** A solution of 0.225 g (1.665 mmol) sulfonyl chloride in 10 mL of dry CH_2Cl_2 was added dropwise to 0.312 g (1.464 mmol) of **2**. The yellowish mixture was stirred at room temperature for 30 minutes. The solvent and the methanesulfonyl chloride (by-product) were removed under reduced pressure. The starting material was completely converted, affording a yellowish brown chloromethyl ether. The crude compound was characterized by ^1H NMR. ^1H NMR (CDCl_3) δ : 8.12 (dd, $J_1 = 1.1$, $J_2 = 8.2$, 1H), 7.75 (d, $J = 7.8$, 1H), 7.67 (dt, $J_1 = 1.1$, $J_2 = 7.4$, 1H), 7.49 (dt, $J_1 = 3.2$, $J_2 = 7.9$, 1H), 5.64 (s, 2H), 5.15 (s, 2H).

2-[(2-Nitrobenzyloxy)methyl]thio}benzothiazole (4). A solution of 2-mercaptobenzothiazole (0.997 g, 5.959 mmol) in 25 mL of DMF was cooled to 0 °C in an ice bath, followed by the addition of 0.358 g (14.929 mmol) of NaH (60% dispersion in mineral oil). The crude product containing the chloromethyl ether was added dropwise to the cooled solution over a 5 minute period and the mixture was stirred at room temperature for 1 h. The reaction was quenched with 20 mL of saturated NH_4Cl . The organic layer was extracted three times with 75 mL of ethyl

acetate, dried over MgSO_4 and the solvent was removed under reduced pressure. Purification was achieved by flash column chromatography using hexanes-ethyl acetate (70:30). Yield = 0.463 g (52%) from 0.578 g of **2**; viscous white liquid; $R_f = 0.51$; ^1H NMR (CDCl_3) δ : 8.06 (dd, $J_1 = 1.2$ Hz, $J_2 = 8.2$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.76 (d, $J = 7.9$ Hz, 2H), 7.60 (dt, $J_1 = 1.2$ Hz, $J_2 = 7.5$ Hz, 1H), 7.42 (dt, $J_1 = 0.9$ Hz, $J_2 = 7.2$ Hz, 2H), 7.31 (dt, $J_1 = 1.1$ Hz, $J_2 = 7.7$ Hz, 1H), 5.59 (s, 2H), 5.15 (s, 2H); ^{13}C NMR (CDCl_3) δ : 165.03, 153.30, 147.66, 136.03, 134.22, 134.12, 129.33, 128.99, 128.68, 126.63, 125.20, 122.44, 121.41, 75.11, 68.73.

2-[(2-nitrobenzyloxy)methyl]sulfonyl}benzothiazole (5**)**. To a solution containing 0.463 g (1.4 mmol) of 2-[(2-nitrobenzyloxy)methyl]thio}benzothiazole in 25 mL of MeOH was added 0.254 g of Na_2WO_4 at 0 °C, followed by 1 mL of H_2O_2 . The reaction was stirred at room temperature for 20 h, after which it was quenched with 25 mL of 0.56 M $\text{Na}_2\text{S}_2\text{O}_5$. The lower organic layer was extracted three times with CH_2Cl_2 , dried over MgSO_4 and the solvent was evaporated at reduced pressure. Purification was done by flash column chromatography using hexanes-ethyl acetate (70:30). Yield = 0.487g (96%) from 0.463 g of **4**. White solid; mp 103-104 °C; $R_f = 0.3$; ^1H NMR (CDCl_3) δ : 8.25 (d, $J = 8.3$, 1H), 8.07 (d, $J = 8.1$, 1H), 8.03 (d, $J = 7.8$, 1H), 7.67 – 7.60 (m, 4H), 7.46(t, $J = 7.7$, 1H), 5.36 (s, 2H), 5.17 (s, 2H); ^{13}C NMR (CDCl_3) δ : 164.2, 152.8, 147.1, 137.2, 133.8, 132.3, 129.1, 128.8, 128.2, 127.8, 125.7, 125.0, 122.3.

General procedure for the synthesis of enol ethers

The carbonyl compound (1.1 mmol, 3 eq) and **5** (0.37 mmol, 1.0 eq) were mixed with 3 mL of dry THF. The solution was cooled to 0 °C in an ice bath, after which 1 mL of LiHMDS was added dropwise over a 1 minute period. The reaction was stirred at 0 °C for 5 h, quenched with 10 mL of saturated NH_4Cl and the organic layer was extracted three times with 25 mL of ethyl acetate. The extract was dried over MgSO_4 , filtered and the solvent was removed under

reduced pressure. The crude vinyl ethers were purified by column chromatography, using CH₂Cl₂ as elutant.

2-nitrobenzyl diphenylacetaldehyde enol ether (1a): Yield: 0.062g (62%) from 0.112 g of **5**, Yellow liquid; ¹H NMR (CDCl₃) δ: 8.18 – 7.28 (m, 14H), 6.62 (s, 1H), 5.42 (s, 2H); ¹³C NMR (CDCl₃) δ: 144.4, 140.2, 137.7 134.5, 134.3, 130.2, 130.1, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 127.1, 126.9, 125.2, 122.4, 72.0; EI-MS, m/z (rel. intensity) 331 (M⁺, 0.1), 302 (23.2), 286 (6.3), 256 (7.6), 239 (4.0), 195 (26.4), 183 (26.3), 167 (100), 165 (39.7), 152 (22.3), 121 (13.4), 105 (54.6), 91 (19.7), 77 (14.7), 65 (3.5), 51 (4.0).

2-nitrobenzyl 2-phenylpropionaldehyde enol ether (1b): Mixture of *cis* and *trans* (2:1). Yield: 97% (0.097 g from 0.136 g of **5**, yellow liquid; ¹H NMR (CDCl₃) δ: 8.17 – 7.20 (m, mixture of *cis* and *trans*, 27H), 6.56 (s, 1H, *trans*), 6.25 (s, 1H, *cis*), 5.37 (s, 2H, *trans*), 5.33 (s, 2H, *cis*), 2.13 (s, 3H, *trans*), 1.97 (s, 3H, *cis*); ¹³C NMR (CDCl₃) δ: 143.7, 142.9, 140.5, 138.5, 135.1, 135.0, 134.5, 134.4, 128.8, 128.7, 128.7, 128.6, 128.4, 128.0, 126.7, 126.6, 125.5, 125.3, 125.3, 116.5, 113.2, 71.8, 71.4, 30.1, 18.8, 13.1; EI-MS, m/z (rel. intensity) 270 (M+1, 1.1), 269 (M⁺, 5.9), 240 (5.2), 224 (5.0), 206 (4.0), 194 (5.0), 180 (9.2), 165 (4.6), 152 (3.6), 136 (83.8), 133 (25.0), 121 (26.5), 105 (100), 91 (12.6), 77 (24.7), 65 (6.5), 51 (7.4).

2-nitrobenzyl 2-*o*-tolylpropionaldehyde enol ether (1c): Mixture of *cis* and *trans* (6:1) Yield: 0.048 g (51%) from 0.121 g of **5**, yellow liquid; ¹H NMR (CDCl₃) (major isomer) δ: 8.11-7.16 (m, 8H, *cis*), 6.14 (s, 1H, *cis*), 5.19 (s, 2H, *cis*), 2.32 (s, 3H, *cis*), 1.85 (s, 3H, *cis*); ¹³C NMR (CDCl₃) δ: 146.6, 143.4, 140.6, 140.5, 139.1, 135.8, 134.9, 133.8, 130.9, 129.8, 129.4, 128.4, 128.4, 128.2, 127.9, 126.8, 125.5, 124.9, 124.7, 116.9, 115.6, 70.5, 70.4, 29.6, 22.6, 20.0, 19.7, 19.5, 19.5, 15.3, 14.1; EI-MS, m/z (rel. intensity) 264 (M+1, 0.5), 283 (M⁺, 3.4), 147 (17.6), 136 (100), 119 (58.8), 91 (22.7), 78 (20.1), 65 (6.0), 51 (2.9).

2-nitrobenzyl 2-(4-Methoxyphenyl)propionaldehyde enol ether (1d): Mixture of *cis* and *trans* (1:1). Yield: 0.022 g (27%) from 0.101 g of **5**, yellow liquid; ^1H NMR (CDCl_3) δ : 8.16-7.24 (m, 16H, *cis* & *trans*), 6.47 (s, 1H, *trans*), 6.18 (s, 1H, *cis*), 5.34 (s, 2H, *trans*), 5.31 (s, 2H, *cis*), 3.84 (s, 3H, *trans*), 3.81 (s, 3H, *cis*), 2.10 (s, 3H, *trans*), 1.93 (s, 3H, *cis*); ^{13}C NMR (CDCl_3) δ : 158.7, 158.4, 147.2, 142.6, 141.9, 135.3, 135.2, 134.4, 134.3, 133.1, 131.1, 129.2, 128.8, 128.6, 128.5, 126.6, 125.3, 125.2, 116.2, 114.2, 113.8, 112.7, 71.7, 71.2, 55.7, 55.6, 18.8, 13.5; EI-MS, m/z (rel. intensity) 300 ($M+1$, 1.5), 299 (M^+ , 5.7), 270 (19.7), 236 (4.4), 210 (13.7), 178 (6.7), 163 (100), 151 (5.3), 146 (7.0), 135 (89.6), 120 (7.5), 91 (12.0), 77 (13.8), 65 (8.2).

2-nitrobenzyl cyclohexanecarboxaldehyde enol ether (1e): Yield: 0.088 g (82%) from 0.159 g of **5**, yellow liquid; ^1H NMR (CDCl_3) δ : 8.10 (dd, $J_1 = 1.2$ Hz, $J_2 = 8.2$ Hz, 1H), 7.80 (dd, $J_1 = 0.9$ Hz, $J_2 = 7.8$ Hz, 1H), 7.68 (td, $J_1 = 1.2$ Hz, $J_2 = 7.5$ Hz, 1H), 7.50 (td, $J_1 = 0.7$ Hz, $J_2 = 4.5$ Hz, 1H), 5.87 (s, 1H), 5.17 (s, 2H), 2.29 (t, $J = 5.5$ Hz, 2H), 1.97 (t, $J = 5.6$ Hz, 2H), 1.54 (m, 6H); ^{13}C NMR (CDCl_3) δ : 147.3, 137.4, 135.6, 134.2, 128.9, 128.4, 125.2, 120.7, 70.6, 30.9, 28.7, 27.4, 27.2, 26.2; EI-MS, m/z (rel. intensity) 248 ($M+1$, 0.5), 247 (M^+ , 3.0), 136 (100), 120 (18.9), 105 (2.1), 93 (7.0), 92 (7.9), 78 (17.0), 67 (5.9), 55 (6.5).

3-(2-nitrobenzyloxy)cyclohex-2-enone (1f): Synthesized as per procedure described in reference 13. Yield: 0.287 g (27%) from 0.945 g of 2-nitrobenzyl bromide, yellow oil; ^1H NMR (CDCl_3) δ : 8.16 (d, $J_1 = 8.3$ Hz, 1H), 7.70 (m, 2H), 7.54 (m, 1H), 5.49 (s, 1H), 5.33 (s, 2H), 2.53 (t, $J = 6.3$ Hz, 2H), 2.39 (t, $J = 6.5$ Hz, 2H), 2.04 (q, $J = 6.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ : 198.6, 175.8, 146.4, 133.1, 130.6, 128.3, 127.9, 124.4, 103.2, 66.3, 35.9, 28.0, 20.4; EI-MS, m/z (rel. intensity) 248 ($M+1$, 0.3), 247 (M^+ , 1.9), 230 (3.0), 217 (1.7), 201 (5.0), 161 (1.8), 136 (100), 120 (3.1), 105 (5.6), 89 (9.0), 78 (54.2), 69 (9.4), 65 (5.7), 51 (3.3).

General procedure for photolysis

A 3.175 mM solution of vinyl ether was prepared in dry CH₃CN in a 50 mL pyrex test tube. Photolysis was done using a Rayonet photochemical reactor with 350 nm light. The reaction was followed by TLC, and the irradiation was stopped after 2h 45 min. The product mixture was then analyzed by GC-MS and the products were identified by their mass spectra and retention times. For the photolysis carried out in the presence of oxygen, the reaction mixture was purged with O₂ during the photolysis. For the photolysis carried out in the absence of oxygen, the reaction mixture was purged with N₂ gas, passed through CaCl₂ (to remove moisture) and BASF catalyst (Aceglass, to remove traces of CO₂ and O₂), for 30 minutes prior to and during the photolysis to ensure efficient removal of oxygen.

The benzophenone released from the photolysis of **1a** was isolated by solvent removal under reduced pressure followed by silica gel column chromatography with ethyl acetate-hexane mixtures. The benzophenone obtained was identified by ¹H NMR and GC-MS.

Control Experiments:

1) A 1.753 mM solution of diphenyl acetaldehyde (0.009 g in 25 mL CH₃CN) was mixed with 0.013 g of 2-nitrobenzyl alcohol and photolyzed for 1h 30 minutes under O₂. There was no evidence of decomposition of diphenylacetaldehyde to benzophenone as observed in reference 12.

2) Photolysis of **1b** in CD₃CN in NMR tube for 30 minutes under air resulted in formation of acetophenone (identified by the singlet at δ 2.5 ppm due to the CH₃ group). This experiment revealed that the oxidative cleavage products were produced by the photochemical process and is not due to thermal decomposition of the photoproducts in the GC column or by hydrolysis during the work up.