Supporting Information

BF$_3$·OEt$_2$ Catalyzed Reaction of Donor-Acceptor Cyclobutanes with Terminal Alkynes: Single Step Access to 2,3-Dihydrooxepines

Ben P. Machin and Brian L. Pagenkopf

Department of Chemistry, The University of Western Ontario
London, ON, N6A 5B7, Canada
bpagenko@uwo.ca

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1. General information

All reactions were run under an argon atmosphere. Flasks were either flame dried under vacuum or dried overnight in an oven and allowed to cool in a desiccator prior to use. Solvents and reagents were purified by standard methods.$^1$ 1,2-Dichloroethane was stored under nitrogen in a Schlenk flask. Bestmann-Ohira reagent was synthesized according to a literature procedure.$^2$ Cyclobutane-1,1-diesters were synthesized according to literature procedure.$^3$ Reaction mixtures were stirred using a magnetic stir bar. Reaction progress was monitored by thin layer chromatography (TLC) performed on F$_{254}$ silica gel plates. The plates were visualized by UV light (254 nm) or by staining with KMnO$_4$ or ceric ammonium molybdate (CAM).$^4$ Column chromatography was performed according to the Still method$^5$ with Silica Flash P60 60 Å silica gel that was purchased from Silicycle.

$^1$H and $^{13}$C NMR data was obtained on a 400 or 600 MHz spectrometer. The spectra obtained were obtained in deuterated chloroform and referenced to residual chloroform signal at $\delta$ 7.25 ppm for $^1$H spectra and the center peak of the triplet at $\delta$ 77.0 ppm for $^{13}$C spectra. The following
abbreviations are used for when multiplicities are given: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; m, multiplet; app, apparent. EI mass spectra were obtained on a Finnigan MAT 8200 spectrometer at an ionizing voltage of 70 eV.

2. Experimental Procedure:

General Procedure for the Preparation of Alkynes: To a solution of aldehyde (1 equiv) in MeOH (0.1 M) was added K$_2$CO$_3$ (1.5 equiv) and Bestmann-Ohira reagent (1.5 equiv). After 18 h, a half saturated solution of NaHCO$_3$ was added and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 10 mL). The organic extracts were combined and washed with brine dried over MgSO$_4$, filtered through a pad of celite and concentrated in vacuo. The resulting residue was purified by flash column chromatography (9:1 hexanes/EtOAc) to afford the corresponding alkyne.

1-ethynyl-4-methyl benzene: The title compound was prepared according to the general procedure for preparation of alkynes, to provide the alkyne as a yellow oil (103 mg, 71%). R$_f$ 0.83 (9:1 hexanes/EtOAc). $^1$H and $^{13}$C NMR data is consistent with previously reported literature values.

1-bromo-4-ethynyl benzene: The title compound was prepared according to the general procedure for preparation of alkynes, to provide the alkyne as an orange solid (270 mg, 68%). R$_f$ 0.78 (4:1 hexanes:EtoAc). $^1$H and $^{13}$C NMR data is consistent with previously reported literature values.

1-ethynylnapthalene: The title compound was prepared according to the general procedure for preparation of alkynes, to provide the alkyne as a dark brown oil (436 mg, 95%). R$_f$ 0.82 (9:1 hexanes:EtoAc). $^1$H and $^{13}$C NMR data are consistent with previously literature values.

1-ethynyl-4-methoxy benzene: The title compound was prepared according to the general procedure for preparation of alkynes, to provide terminal alkyne as a yellow oil (257 mg, 76%). R$_f$ 0.85 (9:1 hexanes/EtOAc). $^1$H and $^{13}$C NMR data are consistent with previously reported values.

1-ethynyl-4-nitro benzene: The title compound was prepared according to the general procedure for preparation of alkynes, to provide the alkyne was an off-white solid (294
mg, 95 %) Rf 0.80 (9:1 hexanes:EtOAc). 1H and 13C NMR data are consistent with previously reported values.7

1-ethyl-4-iodobenzene: (4-iodophenyl)methanol was prepared according to a literature procedure from methyl 4-iodobenzoate11 as an orange solid (456 mg, 95 %). To a solution of (4-iodophenyl)methanol (392 mg, 1.68 mmol, 1 equiv) in EtOAc (4 mL) was added 2-iodoxybenzoic acid (1.43 g, 5.11 mmol, 3 equiv) and the reaction heated to 80 °C. Once the alcohol had been consumed by TLC (2 h), the reaction was cooled to 0 °C in an ice bath and stirred for 1 h. The precipitate was filtered through a pad of celite and the filtrate concentrated in vacuo. The crude reaction product was purified by flash column chromatography afford 4-iodobenzaldehyde (389 mg, 96 %) as an orange solid. The aldehyde was then subjected to the general procedure for preparation of alkynes, to provide the alkyne (360 mg, 94 %) as an orange solid. Rf 0.83 (9:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.66 (d, J = 8.8 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 3.12 (s, 1H); 13C NMR (150 MHz, CDCl3) δ 137.5 (2), 133.6 (2), 121.6, 94.8, 82.7, 78.6; HRMS m/z 227.9429 (calcd for C8H5I 227.9436).

4-ethylphenyl acetate: 4-ethylphenol was prepared from a literature procedure from tert-butyl(4-ethynylphenoxy)dimethylsilane.12 Crude 4-ethylphenol was acetylated according to a literature procedure13 to give the title compound (88 mg, 47 %) as a clear oil. Rf 0.62 (4:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.49 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 3.05 (s, 1H), 2.29 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 169.0, 150.8, 133.3 (2), 121.6 (2), 119.7, 82.8, 77.2, 21.1; HRMS m/z 160.0530 (calcd for C10H8O2 160.0524).

9-ethylanthracene: The title compound was prepared according to a literature procedure14 as an off-white solid (89 mg, 70 %). Rf 0.73 (9:1 hexanes:EtOAc); 1H NMR (600 MHz, CDCl3) δ 8.60 (d, J = 8.2 Hz, 2H), 8.44 (s, 1H), 8.00 (d, J = 8.2 Hz, 2H), 7.60 (t, J = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 4.00 (s, 1H); 13C NMR (150 MHz, CDCl3) δ 133.1, 131.0, 128.6 (2), 128.2, 126.8 (2), 126.5 (2), 125.6 (2), 116.0, 88.2, 80.3; HRMS m/z 202.0786 (calcd for C16H10 202.0783).

tert-butyl(4-ethylphenoxo)dimethylsilane: 4-hydroxybenzaldehyde was protected using a TBS group following a literature procedure15 to afford 4-(tert-butyldimethylsiloxy)benzaldehyde (2.0 g, 96 %) as a yellow oil. 4-(tert-butyldimethylsiloxy)benzaldehyde was converted to the title compound by a Corey-Fuchs reaction following a literature procedure16 (943 mg, 80 % over two steps) as a yellow oil. Rf 0.92 (9:1 hexanes:EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.36 (d, J = 8.2 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 2.98 (s, 1H), 0.97 (s, 9H), 0.19 (s, 6H); 13C NMR (150 MHz, CDCl3) δ 156.3, 133.6 (2), 120.1 (2), 114.8, 83.7, 75.9, 25.6, -4.4; HRMS m/z 232.1278 (calcd for C14H20O2Si 232.1283).
3-ethynyl-1-tosyl-1H-indole: 1-tosyl-1H-indole-3-carbaldehyde was prepared from indole-3-carbaldehyde by a literature procedure to afford an off-white solid (2.18 g, 7.3 mmol, 75%). The title compound was prepared from 1-tosyl-1H-indole-3-carbaldehyde following a literature procedure to afford 3-ethynyl-1-tosyl-1H-indole (932 mg, 72 %) as a light brown solid. Rf 0.81 (9:1 hexanes/EtOAc). H and 13C NMR data are consistent with previously reported values.

General procedure for the BF3·OEt2 catalyzed reaction of cyclobutane-1,1-diesters with alkynes: To a solution of cyclobutane 1 (0.4 mmol, 1 equiv) and alkyne (1.1 equiv) in 1,2-dichloroethane (6 mL, 0.1 M) was added BF3·OEt2 (50 μL, 0.4 mmol, 1 equiv). A reflux condenser was quickly attached and the flask was placed in a pre-heated oil bath. After complete consumption of the cyclobutane as indicated by TLC (5 – 15 min), the reaction mixture was poured into a separatory funnel containing a half saturated solution of NaHCO3. The aqueous phase was extracted with CH2Cl2 (3 x 5 mL) and the combined organic extracts were washed with brine, dried over MgSO4, filtered through a pad of celite and concentrated in vacuo. The crude reaction product was purified by flash column chromatography (4:1 hexanes/EtOAc) to provide the corresponding addition-rearrangement products.

diethyl 2-(((4Z,6Z)-7-phenyl-2,3-dihydrooxepin-4-yl)methyl) malonate (4a): The title compound was prepared according to the general reaction procedure to afford a yellow oil (79 mg, 53 %). Rf 0.49 (4:1 hexanes/EtOAc); H NMR (600 MHz, CDCl3) δ 7.56 – 7.55 (m, 2H), 7.31 – 7.29 (m, 2H), 7.27 – 7.25 (m, 1H), 5.72 (d, J = 8.8 Hz, 1H), 5.53 (d, J = 8.8 Hz, 1H), 4.32 (app t, J = 4.1 Hz, 2H), 4.19 (q, J = 7.0 Hz, 4H), 3.55 (t, J = 7.9 Hz, 1H), 2.73 (d, J = 8.2 Hz, 2H), 2.62 (app t, J = 4.1 Hz, 2H), 1.25 (t, J = 7.0 Hz, 6H); 13C NMR (100 MHz, CDCl3) δ 169.0 (2), 157.4, 137.5, 137.0, 128.3 (2), 128.1, 125.3 (2), 122.1, 99.1, 69.0, 61.5 (2), 51.0, 38.8, 37.1, 14.1 (2); HRMS m/z 344.1617 (calcd for C20H24O5).

diethyl 2-(((4Z,6Z)-7-p-tolyl-2,3-dihydrooxepin-4-yl)methyl) malonate (4b): The title compound was prepared according to the general reaction procedure to afford a yellow oil (50 mg, 35 %). Rf 0.47 (4:1 hexanes/EtOAc); H NMR (400 MHz, CDCl3) δ 7.45 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 7.8 Hz, 2H), 5.70 (d, J = 8.2 Hz, 1H), 5.49 (d, J = 8.2 Hz, 1H), 4.31 (app t, J = 4.3 Hz, 2H), 4.18 (q, J = 7.2 Hz, 4H), 3.55 (t, J = 8.0 Hz, 1H), 2.72 (d, J = 7.8 Hz, 2H), 2.61 (app t, J = 4.1 Hz, 2H), 2.33 (s, 3H), 1.25 (t, J = 7.0 Hz, 6H); 13C NMR (100 MHz, CDCl3) δ 169.0 (2), 157.6, 138.0, 136.9, 134.2, 128.8 (2), 125.2 (2), 122.2, 98.4, 69.0, 61.4 (2), 51.1, 38.8, 37.1, 21.2, 14.1 (2); HRMS m/z 358.1767 (calcd for C21H26O5).
diethyl 2-(((4Z,6Z)-7-(4-bromophenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4c): The title compound was prepared according to the general reaction procedure to afford a yellow oil (57 mg, 34%). Rf 0.48 (4:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.42 (s, 4H), 5.70 (d, J = 7.6 Hz, 1H), 5.52 (d, J = 8.2 Hz, 1H), 4.30 (app t, J = 4.1 Hz, 2H), 4.18 (q, J = 7.2 Hz, 4H), 3.54 (t, J = 7.9 Hz, 1H), 2.72 (d, J = 8.2 Hz, 2H), 2.61 (app t, J = 4.1 Hz, 2H), 1.25 (t, J = 6.7 Hz, 6H); 13C NMR (150 MHz, CDCl3) δ 168.9 (2), 156.3, 138.2, 135.9, 131.2 (2), 126.8 (2), 122.0, 121.9, 99.5, 69.0, 61.5 (2), 51.0, 38.7, 37.1, 14.1 (2); HRMS m/z 422.0731 (calcd for C20H23BrO5 422.0729).

diethyl 2-(((4Z,6Z)-7-(4-iodophenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4d): The title compound was prepared according to the general reaction procedure to afford a yellow oil (67 mg, 36%). Rf 0.58 (4:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.61 (d, J = 8.8 Hz, 2H), 7.28 (d, J = 8.8 Hz, 2H), 5.69 (d, J = 8.2 Hz, 1H), 5.52 (d, J = 8.2 Hz, 1H), 4.29 (app t, J = 4.1 Hz, 2H), 4.18 (q, J = 7.0 Hz, 4H), 3.54 (t, J = 7.9 Hz, 1H), 2.72 (d, J = 7.6 Hz, 1H), 2.60 (app t, J = 4.1 Hz, 2H), 1.24 (t, J = 7.0 Hz, 6H); 13C NMR (150 MHz, CDCl3) δ 168.9 (2), 156.3, 138.3, 137.2 (2), 136.5, 127.0 (2), 121.8, 99.5, 93.6, 69.0, 61.4 (2), 51.0, 38.7, 37.4, 14.1 (2); HRMS m/z 470.0598 (calcd for C20H23IO5 470.0590).

diethyl 2-(((4Z,6Z)-7-(napthalen-1-yl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4e): The title compound was prepared according to the general reaction procedure to afford a yellow oil (58 mg, 35%). Rf 0.50 (4:1 hexanes/EtOAc); 1H NMR (400 MHz, CDCl3) δ 8.09 (d, J = 7.8 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.55 – 7.45 (m, 3H), 7.44 – 7.39 (m, 1H), 5.73 (d, J = 8.6 Hz, 1H), 5.26 (d, J = 8.2 Hz, 1H), 4.45 (app t, J = 4.3 Hz, 2H), 4.23 (q, J = 7.0 Hz, 4H), 3.60 (t, J = 7.8 Hz, 1H), 2.77 (d, J = 8.2 Hz, 2H), 2.71 (app t, J = 4.3 Hz, 2H), 1.29 (t, J = 7.2 Hz, 6H); 13C NMR (100 MHz, CDCl3) δ 169.0 (2), 158.4, 137.3, 136.3, 133.7, 131.8, 128.8, 128.2, 126.6, 126.0, 125.8, 125.7, 125.0, 122.1, 103.5, 69.0, 61.5 (2), 51.0, 38.7, 37.2, 14.1 (2); HRMS m/z 394.1772 (calcd for C24H26O5 394.1780).

diethyl 2-(((4Z,6Z)-7-(4-acetoxyphenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4f): The title compound was prepared according to the general reaction procedure to afford a yellow oil (63 mg, 35%). Rf 0.35 (4:1 hexanes/EtOAc); 1H NMR (600 MHz, CDCl3) δ 7.56 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 5.70 (d, J = 8.2 Hz, 1H), 5.49 (d, J = 8.8 Hz, 1H), 4.30 (app t, J = 4.3 Hz, 2H), 4.18 (q, J = 7.0 Hz, 4H), 3.54 (t, J = 7.9 Hz, 1H), 2.72 (d, J = 7.6 Hz, 2H), 2.61 (app t, J = 4.1 Hz, 2H), 2.28 (d,
diethyl 6-(4-(tert-butyldimethylsilyloxy)phenyl)-2,3,3a,4-tetrahydrobenzofuran-5,5(7aH)-dicarboxylate (5): The title compound was prepared according to the general reaction procedure to afford a yellow oil (38 mg, 20%). R_f 0.60 (4:1 hexanes/EtOAc); ^1H NMR (600 MHz, CDCl_3) δ 7.25 (d, J = 7.6 Hz, 2H), 6.70 (d, J = 8.8 Hz, 2H), 6.08 (d, J = 3.5 Hz, 1H), 4.30 (q, J = 7.0 Hz, 2H), 4.19 – 4.15 (m, 2H), 4.01 – 3.98 (m, 1H), 3.86 – 3.81 (m, 1H), 2.39 (dd, J = 12.6, 4.4 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.26 – 2.21 (m, 1H), 2.04 – 1.96 (m, 1H), 1.31 (t, J = 7.3 Hz, 3H), 1.31 (t, J = 7.3 Hz, 3H), 0.94 (s, 9H), 0.82 (t, J = 7.0 Hz, 3H), 0.14 (s, 6H); ^13C NMR (100 MHz, CDCl_3) δ 170.6, 170.4, 155.1, 140.2, 133.3, 127.4, 119.4 (2), 74.0, 66.9, 61.8, 61.4, 60.8, 34.8, 33.0, 32.9, 25.7, 18.2, 14.1, 13.5, -4.5; HRMS m/z 474.2448 (calcd for C_{26}H_{38}O_{6}Si 474.2438).

References

1-ethynyl-4-iodobenzene
1-ethynyl-4-iodobenzene

$^{13}$C NMR, 150 MHz, CDCl$_3$
4-ethynylphenyl acetate

\[
\text{AcO} \quad 4-\text{ethynylphenyl acetate}
\]
4-ethynylphenyl acetate

AcO

13C NMR, 150 MHz, CDCl$_3$
9-ethynylanthracene

'H NMR, 600 MHz, CDCl₃
9-ethynylanthracene

$\text{C NMR, 150 MHz, CDCl}_3$

S 12 of S 29
**tert-butyl(4-ethynylphenoxy)dimethylsilane**

\[
\begin{align*}
\text{TBSO} & \quad \text{-}7.37 \\
\text{6.76} & \quad 0.88 \\
\text{10.34} & \quad 0.19
\end{align*}
\]

\( ^1H \text{ NMR, 600 MHz, CDCl}_3 \)
tert-butyl(4-ethynylphenoxy)dimethylsilane

\[ \text{Chemical Shift (ppm)} \]

\[
\begin{align*}
-156.3 & \\
-133.6 & \\
-120.1 & \\
-114.8 & \\
-83.7 & \\
-75.9 & \\
-25.6 & \\
\end{align*}
\]

\[ ^{13} \text{C NMR, 150 MHz, CDCl} _3 \]

S 14 of S 29
diethyl 2-(((4Z,6Z)-7-phenyl-2,3-dihydrooxepin-4-yl)methyl)malonate (4a)
diethyl 2-(((4Z,6Z)-7-phenyl-2,3-dihydrooxepin-4-yl)methyl)malonate (4a)

\[
\text{C NMR, 150 MHz, CDCl}_3
\]
diethyl 2-(((4Z,6Z)-7-p-tolyl-2,3-dihydrooxepin-4-yl)methyl)malonate (4b)
diethyl 2-(((4Z,6Z)-7-p-tolyl-2,3-dihydrooxepin-4-yl)methyl)malonate (4b)

$\text{^{13}C NMR, 100 MHz, CDCl}_3$
diethyl 2-(((4Z,6Z)-7-(4-bromophenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4c)

\[ \text{Br} \]

\[ \text{CO}_2\text{Et} \]

\[ \text{CO}_2\text{Et} \]

\[ ^1\text{H NMR, 600 MHz, CDCl}_3 \]

S 20 of S 29
diethyl 2-(((4Z,6Z)-7-(4-bromophenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4c)

\[
\begin{align*}
\text{Br} & \quad \text{CO}_2\text{Et} \\
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et}
\end{align*}
\]

\(13\text{C NMR, 150 MHz, CDCl}_3\)

S 21 of S 29
diethyl 2-(((4Z,6Z)-7-(4-iodophenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4d)

\[ \text{H NMR, 600 MHz, CDCl}_3 \]
diethyl \((4Z,6Z)-7-(4\text{-iodophenyl})-2,3\text{-dihydrooxepin-4-yl})\text{methyl} \text{malonate} \ (4d)
diethyl 2-(((4Z,6Z)-7(naphthalen-1-yl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4e)
diethyl 2-(((4Z,6Z)-7(naphthalen-1-yl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4e)

13C NMR, 100 MHz, CDCl₃
diethyl 2-(((4Z,6Z)-7-(4-acetoxyphenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4f)

\[
\text{AcO} \\
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Et}
\]

\[\begin{align*}
\text{H NMR, } 400 \text{ MHz, CDCl}_3
\end{align*}\]
diethyl 2-(((4Z,6Z)-7-(4-acetoxyphenyl)-2,3-dihydrooxepin-4-yl)methyl)malonate (4f)
diethyl 6-(4-(tert-butyldimethylsiloxy)phenyl)2,3,3a,4,5,5(7aH)-tetrahydrobenzofuran-5,5-dicarboxylate (5)
diethyl 6-(4-(tert-butyl dimethylsiloxy)phenyl)2,3,3a,4,-tetrahydrobenzofuran-5,5(7aH)-dicarboxylate (5)

\begin{align*}
\text{C NMR, 100 MHz, CDCl}_3
\end{align*}