Angewandte Chemie

Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

for

Angew. Chem. Int. Ed. Z50415

69451 Weinheim, Germany

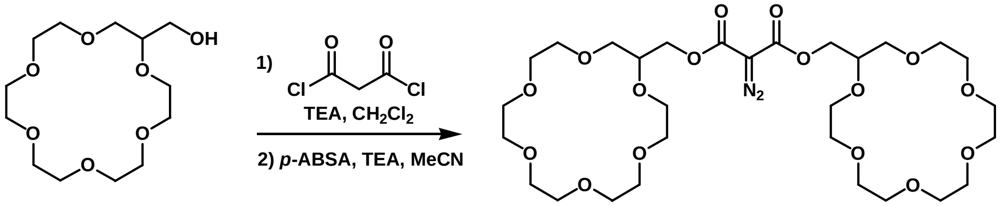
Molecular Mousetraps: Gas Phase Studies of the Covalent Coupling of Non-Covalent Complexes Initiated by Reactive Carbenes Formed by Controlled Activation of Diazo Precursors**

Ryan R. Julian, Jeremy A. May, Brian M. Stoltz,* and J. L. Beauchamp*

* Prof. J. L. Beauchamp, Beckman Institute, California Institute of Technology, Pasadena, California 91125
Fax: (626)-568-8641, Email: jlbchamp@its.caltech.edu

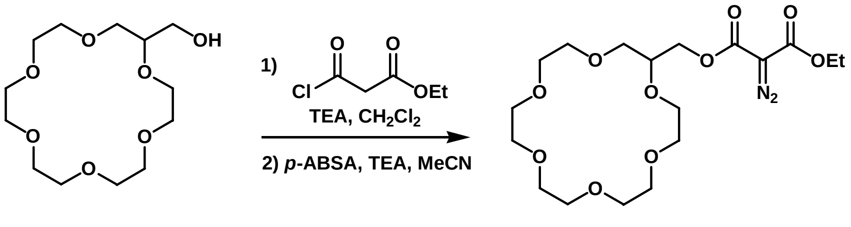
* Prof. Brian M. Stoltz, The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, Email: stoltz@caltech.edu

General Information: Due caution should always be used when handling diazo compounds. Reactions were performed in flame-dried glassware under a nitrogen atmosphere using freshly distilled solvents. All other reagents were used as received from commercial sources. Reaction temperatures were controlled by an IKAmag temperature modulator. ^{1}H NMR spectra were recorded on a Varian Mercury 300 spectrometer (at 300 MHz) and are internally referenced to the chloroform peak (7.27 ppm) relative to Me_4Si. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Preparatory reversed phase HPLC was performed on a Beckman HPLC with a Waters DeltaPak 25 x 100 mm, 100 μm C18 column equipped with a guard.



1

Compound 1: To a stirred, dry solution of 18-crown-6-methanol (50.0 µl, 0.16 mmol), dichloromethane (1.5 ml), and triethylamine (25 µl, 0.18 mmol) was added malonyl dichloride (9.0 µl, 0.09 mmol). The mixture was heated to reflux for eight hours, cooled, and then evaporated *in vacuo*. The residue was dissolved in acetonitrile (1.2 ml), and treated with triethylamine (220 µl, 1.58 mmol). To this solution was added *p*-acetamidobenzenesulfonyl azide (p-ABSA) (31.9 mg, 0.13 mmol), and the mixture was stirred for ten hours. The solvent was removed *in vacuo,* the residue dissolved in a minimal amount of dichloromethane (500 µl), and the undesired salts were precipitated out of solution with the addition of ether (5 ml). Filtration through celite and removal of solvent *in vacuo* yielded **1** (41.8 mg, 81% yield). A small sample (~15 mg) was chromatographed to analytical purity by HPLC, (0.1% (wt/v) TFA in water, 8.0 ml/min, 0.30% acetonitrile/min, 83-85 min). FTIR (thin film) 3429, 2918, 2143, 1743, 1691, 1595, 1454, 1356, 1251, 1108 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.44 (dd, J = 3.85, 11.5 Hz, 1H), 4.26 (dd, J = 5.49, 11.0 Hz, 1H), 3.87-3.58 (m, 23H); ESI-MS *m/z* 683.3 (H^+).



2

Compound 2: To a stirred, dry solution of 18-crown-6-methanol (50.0 µl, 0.16 mmol), dichloromethane (1.5 ml), and triethylamine (33 µl, 0.24 mmol) was added ethyl malonyl chloride (28 µl, 0.22 mmol). The mixture was heated to reflux for eight hours, cooled, and then evaporated *in vacuo*. The residue was dissolved in acetonitrile (750 µl), and treated with triethylamine (30 µl, 0.22 mmol). To this solution was added *p*-acetamidobenzenesulfonyl azide (53.1 mg, 0.22 mmol), and the mixture was stirred for ten hours. The solvent was removed *in vacuo*, the residue dissolved in a minimal amount of dichloromethane (500 µl), and the undesired salts were precipitated out of solution with the addition of ether (5 ml). Filtration through celite and removal of solvent *in vacuo* yielded **2** (59.8 mg, 87% yield). A small sample (~15 mg) was chromatographed to analytical purity by HPLC (0.1% (wt/v) TFA in water, 8.0 ml/min, 0.30% acetonitrile/min, 82-85 min). FTIR (thin film) 2879, 2142, 1755, 1689, 1457, 1326, 1102, 762; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.45 (dd, J = 3.85, 12.1 Hz, 1H), 4.31 (q, J = 7.14 Hz, 2H), 4.27 (m, 1H), 3.85 (t, J = 4.95), 3.80 (s, broad, 1H), 3.67 (s, broad, 21H), 1.32 (t, j = 7.14 Hz, 3H); ESI-MS *m/z* 435.2 (H^+).