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DEPROTECTION OF ACETALS FROM UNSATURATED, UNSTABLE BROMOKETONES

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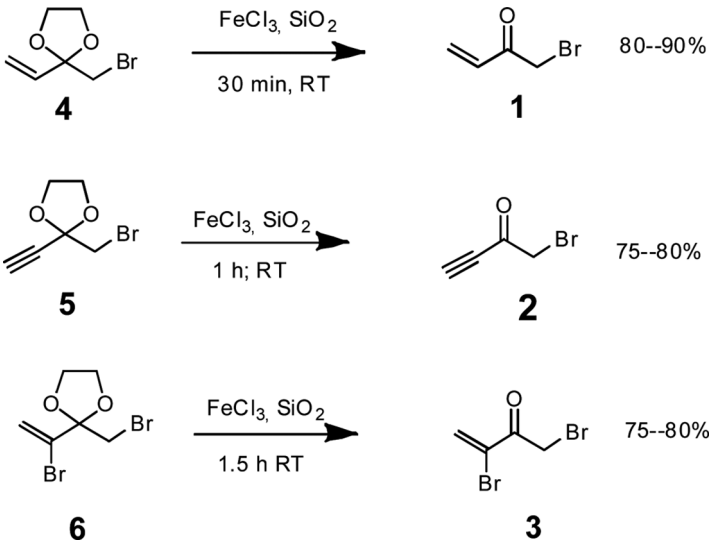
GRAPHICAL ABSTRACT



Abstract *The unstable ketones 1-bromo-3-buten-2-one, 1-bromo-3-butyn-2-one, and 1,3-dibromo-3-buten-2-one can be obtained from the corresponding acetals in high yields by treating the acetals with anhydrous iron (III) chloride suspended on dry silica. A simplified procedure for preparing the reagent is also given.*

Keywords Acetal deprotection; iron (III) chloride; silica; unsaturated bromoketones

INTRODUCTION

This article is complementary to previous communication[1–3] and describes a simplified procedure for liberating unstable bromoketones from their corresponding ethylene acetals. The prepared compounds are shown in Figure 1.

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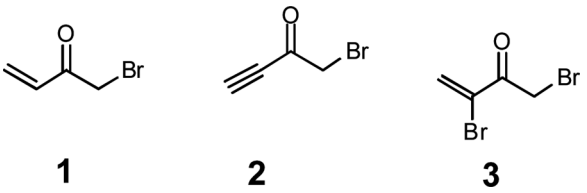
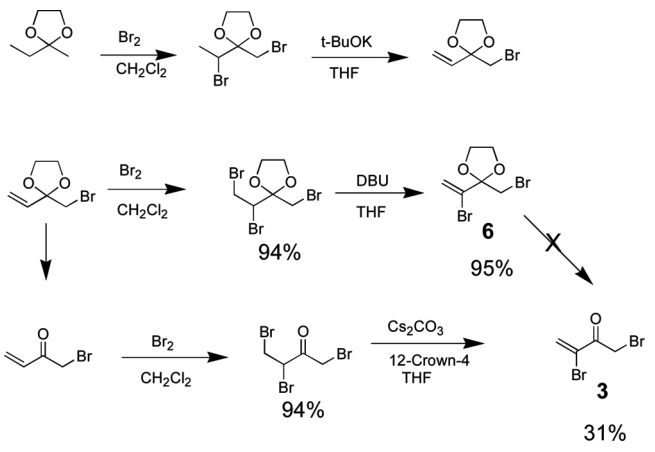


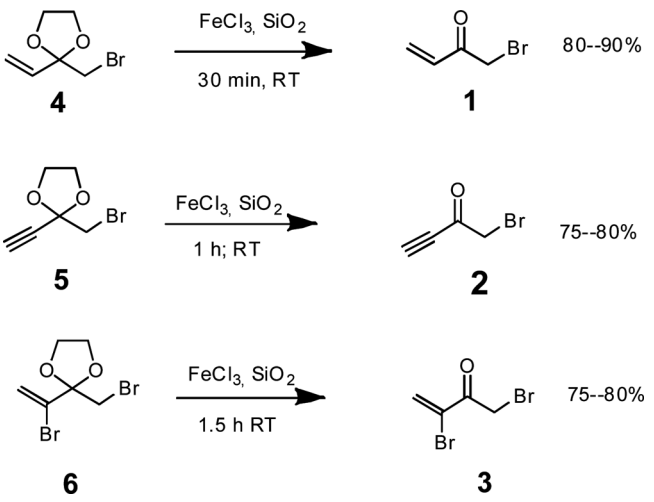
Figure 1. Compounds prepared.

The scope of using these compounds as building blocks in synthesis is not yet fully explored. Reactions of **1** with nucleophilic reagents such as amines, complex hydrides, and stabilized carbanions is described in Westerlund et al.[1] The reaction of **3** with stabilized carbanions gave functionalized cyclopentenons by a conjugate addition, dyhydrobromination, and an intramolecular displacement of the bromine in the bromomethyl group.[2] To the best of our knowledge, the use of **2** in synthetic transformations has not yet been reported.

The synthesis of 1-bromo-3-buten-2-one, **1**, is described in Westerlund and Carlson[3] and Carlson et al.,[4] and the final step is the deacetalization of the ketone. Hydrolysis under acid conditions is inefficient. Formolysis with 98% formic acid afforded the desired transformation in 86% yield. Hydrolysis with 1:1 mixtures of Et_2O/C_5H_{12} and HCO_2H/H_2O under microwave activation was also efficient, and afforded 74% yield. The formolytic conditions could also be used to liberate 1-bromo-3-butyn-2-one, **2**, from the corresponding acetal in 74% yield. However, any attempts to cleave the ethylene acetal, **6**, from 1,3-dibromo-3-buten-2-one, **3**, failed, and this compound was instead obtained by dehydrobromination of 1,3,4-tribromo-2-butanone with lithium carbonate.[3] The yield was very low, 31%, mainly due to rapid polymerization of the unsaturated bromoketone (see Scheme 1). An inefficient method for the synthesis of **3** by bromination of 2-trimethylsiliyloxy-1,3 butadiene has previously been described.[2]



Scheme 1. Synthetic route to **3**.



Scheme 2. Bromoacetals deprotected by $FeCl_3$ on dry silica.

We thought that the procedure for the synthesis of **3** could be improved if it would be possible to cleave the acetal. A procedure for acetal cleavage by using iron (III) chloride on silica has been published.[6] In the published procedure, the reagent is prepared by adding ferric chloride dissolved in acetone to silica, followed by evaporation of the acetone under reduced pressure, then by drying in vacuum at room temperature for several hours. The reagent has also been prepared by stirring silica and iron (III) chloride for 24 h at room temperature.[7] We have found that the reagent can be prepared more rapidly: Dry anhydrous iron (III) chloride is added to dry silica followed by stirring of the mixture magnetically for 1 h on an ice-bath, or for larger batches, by vigorous shaking of the mixture in a stoppered flask. The reagent is a yellow powder and can be used directly for acetal cleavage (see the Experimental for details). See Scheme 2.

The following results were obtained:

EXPERIMENTAL

General

Silica (SiO_2-Davisil RLC14A 35–70, 35–70 μm) and iron (III) chloride reagent grade 97% from Sigma-Aldrich were used. The bromoacetals were prepared according to Mekonnen et al.[5] and Westerlund and Carlson.[3]

Preparation of the Silica-Iron (III) Chloride Reagent

A round-bottomed flame-dried 1 L flask was purged with nitrogen and then charged with 100 g of dry silica and 10.0 g of iron (III) chloride. An egg-shaped, 60 mm magnetic stirring bar was introduced, and the mixture was magnetically stirred on an ice-bath for 1 h.

*Warning! The bromoketones **1**, **2**, and **3** are very powerful lacrymators and can also be expected to be mutagenic. They should be handled with great care.*

Cleavage of the Acetals 4, 5, and 6

The actetal (10.00 g) was dispersed on 30 g of silica and added to the stirred silica-iron (III) chloride reagent by means of a funnel. The mixture was then stirred at $\pm 0^\circ$ for the time given in Scheme 2. Samples of the reaction mixture were withdrawn and analyzed by GLC to ensure a complete conversion. Then, 400 mL of diethyl ether was added, and the resulting heterogeneous mixture was filtered by suction through a sintered glass funnel. The filter cake was washed twice with 100 mL portions of diethyl ether. The combined etheral solutions were washed three times with 200 mL portions of distilled water, and dried over anhydrous magnesium sulfate.

After filtration, ca. 10 mg of magnesium oxide and ca. 10 mg of hydroquinone were added to prevent polymerization, and the ether was removed by evaporation under reduced pressure from a room-temperature water bath. The pressure was regulated to obtain a smooth distillation. Then, the receiver flask was emptied and the evaporation was continued for 15 min at 10 mbar to remove traces of the diethyl ether. The purity of the crude products were >95% (^{1}H NMR), and they can be taken to the next transformation without further purification. The following yields were obtained:

2-Bromomethyl-2-vinyl-1,3-dioxolane, **4**, gave 6.17–6.95 g (80–90%) of 1-bromo-3-buten-2-one, **1**. The reaction time was 0.5 h.

2-Bromomethyl-2-ethynyl-1,3-dioxolane, **5**, gave 5.76–6.15 g (75–80%) of 1-bromo-3-butyn-2-one, **2**. The reaction time was 1 h.

2-Bromomethyl-2-(1-bromoethenyl)-1,3-dioxolane, **6**, gave 6.17–6.95 g (80–90%) of 1-bromo-3-buten-2-one, **3**. The reaction time was 1.5 h.

The ketones undergo polymerization at room temperature, but they can be stored for several days in the freezer. Ketone, **3**, should be stored at $-50\,^\circ$C.

GLC Analyses to Monitor the Reaction

Samples (ca. 100 mg) of the reaction mixture were withdrawn from the reaction mixture with a spoon and transferred into a 2 mL vial. Water (0.5 mL) and diethylether (1 mL) were added, and the mixture was shaken. The etheral layer was withdrawn and filtered through a plug of cotton, and the volume was adjusted to 2 mL. The analyses were made on a Varian 3300 chromatograph equipped with split injector and a flame ionization detector. Specifications were as follows: column: SPB-5, 30 m, 0.35 mm i.d. Injection volume 1 μL; injection temperature, 275 °C; detector temperature, 275 °C; temperature program: 70 °C, 5 min; 10 °C min^{-1}, 180 °C.

Spectroscopic Characterization of 1, 2, and 3

This was reproduced from Westerlund and Carlson[3] and Carlson et al.[4]

General. All ^{1}H and ^{13}C NMR spectra were recorded on a Varian 400 FT-NMR system using $CDCl_3$ as a solvent at room temperature. Chemical shifts

are given in ppm and J-values in Hz. IR spectra were recorded on a FT-IR spectrometer and are reported as wave number. GC-MS spectra were registered on a Hewlett 5890 Packard series II CP Sil 5 CB column (25 m) followed by VG Quattro mass spectrometer. A Finnigan-MAT-95XL mass spectrometer was used to obtain HRMS data, and the spectra were obtained at 250 °C and 70 eV.

1-Bromo-3-buten-2-one, 1. The product is unstable, and it was not possible to send a sample for elemental analysis. Spectral properties are as follows: ^{1}H NMR: δ 4.03 (s, 2H), 5.95 (dd, 1H, $J = 10.6$ Hz, 0.9 Hz), 6.38 (dd. 1H, $J = 17.5$ Hz, Hz, 0.9 Hz), 6.55 (dd, 1H, $J = 17.5$ Hz, 10.6 Hz); ^{13}C NMR: δ = 32.6, 131.1, 133.2, 191.5; IR (neat between NaCl plates) ν_{max}/cm^{-1}: 1690 (C=O), 1620 (C=C–C=O); MS (EI 70 eV): m/z (relative abundance) [Assignment] 150 (78) 148 (77) [M^{+}], 123 (35), 121 (32) [M - vinyl], 95 (100), 93 (99) [CH_2Br+], 79, 69 (60) [M - Br], 55 (92) [M - CH_2Br].

1-Bromo-3-butyn-2-one, 2. ^{1}H NMR: δ 4.05 (s, 2H), 3.41 (s, 1H); ^{13}C NMR: δ177.6, 82.2, 79.1, 35.2: IR (net NaCl plates) ν_{max}, cm^{-1}: 3290, 2250, 2100, 1680; HRMS: observed for C_4H_3BrO: 147.9340; calcd: 147.9347.

1,3-Dibromo-3-buten-2-one, 3. ^{1}H NMR δ 6.92 (d, 1H), j 5.95 (dd, 1H, $J = 2$–7 Hz), 6.45(d. 1H, $J = 2.7$ Hz, 4.33 (s, 2H.); ^{13}C NMR δ 186.1, 131.0, 127.1. 30.1 32.6, 131.1, 133.2, 191.5;;GC/ MS (EI 70 eV) m/z (relative abundance) [Assignment]: 230 (15), 228 (28), 226 (14), 135 (100), 133, 107, (41), 105, 95, 93, 81(12) 79.

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