Convenient Synthesis of Ethyl Triethylsilyldiazoacetate and Stereoselective Preparation of Aliphatic Silylketene Acetals: In situ Formation of Triethylsilyl Perchlorate

Craig S. Wilcox, Robert E. Barston

Department of Chemistry, University of Texas at Austin, Austin, Texas 78712, U.S.A.

Experimental details are reported for the silylation of esters by a method based upon in situ preparation of triethylsilyl perchlorate. The preparation of ethyl triethylsilyldiazoacetate (5) in 99% yield from ethyl diazoacetate (3) is detailed. A preparative procedure for the stereoselective formation of a (Z)-O-silylketene acetal 2b from isopropyl propanoate (1) is described.

Recently, we reported the use of triethylsilyl perchlorate for kinetically controlled silylation of simple aliphatic esters\(^1\) (Scheme A). The process affords silylketene acetals in high yield with good control of geometry. The major product arising from primary and secondary propanoates is of (Z)-configuration, while for t-butyl propanoate, the major isomer is of (E)-configuration\(^2\).

\[ \text{Scheme A} \]

The experiments are easily performed using pure triethylsilyl perchlorate (TESP) which is a distillable, covalent ester of perchloric acid first prepared by Barton and Tully\(^3\). It is important to remember, however, that the use of derivatives of perchloric acid in any form is potentially hazardous, and for this reason a procedure which avoids the isolation of the silyl perchlorate and minimizes the potential risk in this process has been developed.

The reaction of triethyl perchlorate with silanes is well suited for the in situ formation of silyl perchlorates\(^4\). The byproduct of this reaction, triphenylmethane, is inert to the reagents and conditions required for ester silylation, and is easily re-
moved from higher boiling products by elution from a short column of silica with pentane, or from distillable products by distillation. *Trityl perchlorate should be handled with all the precautions due any perchlorate salt."

We report here the preparation of a silylketene acetal 2 from 1 and TESP generated in situ from trityl perchlorate and triethylsilane. Whereas formation of the silyl perchlorate is best achieved in dichloromethane, stereoselectivity in the formation of the acetal is improved in less polar solvents. Therefore the solution of silyl perchlorate is diluted with tetrachloromethane prior to addition of the amine and ester. The workup of these reactions significantly affects the stereochemical outcome and the purity of the product. Tetramethylguanidine is added in order to prevent product isomerization due to proton transfer from the trialkylammonium salt. Methanol is added to quench the small excess of silyl perchlorate. The resulting methysilyl ether is volatile and more easily separated from the desired product than is the disiloxane which is provided by a direct aqueous workup.

In the event, the application of this new process to isopropyl propanoate (1) afforded after fractional distillation 74% of pure silylketene acetics 2a/2b. The major isomer (2a/2b = 7/93) was of (Z)-configuration as evidenced by H-N.M.R. spectroscopy and G.L.C.

![Chemical structure](image)

**Scheme B**

The outcome of the reaction of TESP with ethyl diazoacetate (3) was of interest because two different reactions are feasible between diazoacettes and electrophiles. A priori, (Scheme B) electrophilic silicon derivatives could react through O-silylation and afford the relatively stable alkenylsodium salts 4, or by C-silylation, and generate trialkylsilyldiazoacetates 5 - 9. Both of these products offer intriguing possibilities for use in organic synthesis, and for these reasons the reaction of ethyl diazoacetate with TESP was investigated. The possiblity that the alkenylsodium salt 4 could deprotonate to liberate molecular nitrogen and afford an alkylidene carbene was especially intriguing.

The reaction of TESP (prepared in situ) with ethyl diazoacetate (3) under the same conditions which afford O-silylation with propanoate esters, gave an excellent yield (99%) of ethyl triethylsilyldiazoacetate (5). Silylated diazoacettes have been prepared previously by deprotonation of diazoacetates at low temperature followed by treatment of the resulting lithium derivatives with silyl chlorides, by metal exchange starting with mercury derivatives of ethyl diazooacetate, and through direct reaction of a chlorotrimethylsilane with the diazoester. The present convenient procedure affords higher yields than any previously known method.

Silylation of esters by triethylsilyl perchlorate in the presence of hindered tertiary amines is a very rapid and clean reaction. The substantially improved procedure reported here eliminates the need for isolation of the silyl perchlorate. We are currently exploring the possibility of replacing perchlorate derivatives in this procedure with other less hazardous leaving groups. Ongoing efforts in this laboratory are directed toward an exploration of the synthetic uses of the processes and products described herein.

1H-N.M.R. spectra were recorded on a Varian EM-390 (90 MHz) or Nicolet NT-200 (200 MHz) spectrometers. Chemical shifts are reported as values in parts per million relative to tetramethylsilane as internal standard. Capillary G.L.C. analysis was performed on a Varian 3700 instrument equipped with a 0.25 mm (I.D.) glass column, 25 m in length, wall coated with Carbowax 20M. Injection port temperatures (split ratio 400:1) were typically held at 200°C above the column oven temperature.

Dichloromethane, tetramethylguanidine, and disoproplyphethylamine and isopropyl propanoate were distilled from calcium hydride immediately before use. Chloroform and chloroform-d were filtered through alumina (activity I) immediately prior to use. Triphenylmethyl perchlorate was prepared according to Dauben. Ethyl diazoacetate and triethylsilane (reagent grade commercial products) were used as obtained and without further purification. Dry ether was distilled from sodium metal in the presence of benzenophenone ketyl. Methanol was distilled from sodium.

(1) H-N.M.R. spectra were recorded on a Varian EM-390 (90 MHz) or Nicolet NT-200 (200 MHz) spectrometers. Chemical shifts are reported as values in parts per million relative to tetramethylsilane as internal standard. Capillary G.L.C. analysis was performed on a Varian 3700 instrument equipped with a 0.25 mm (I.D.) glass column, 25 m in length, wall coated with Carbowax 20M. Injection port temperatures (split ratio 400:1) were typically held at 200°C above the column oven temperature.

Dichloromethane, tetramethylguanidine, and disopropylmethylamine and isopropyl propanoate were distilled from calcium hydride immediately before use. Chloroform and chloroform-d were filtered through alumina (activity I) immediately prior to use. Triphenylmethyl perchlorate was prepared according to Dauben. Ethyl diazoacetate and triethylsilane (reagent grade commercial products) were used as obtained and without further purification. Dry ether was distilled from sodium metal in the presence of benzenophenone ketyl. Methanol was distilled from sodium.

**Scheme B**

The outcome of the reaction of TESP with ethyl diazoacetate (3) was of interest because two different reactions are feasible between diazoacetates and electrophiles. A priori, (Scheme B) electrophilic silicon derivatives could react through O-silylation and afford the relatively stable alkenylsodium salts 4, or by C-silylation, and generate trialkylsilyldiazoacetates 5 - 9. Both of these products offer intriguing possibilities for use in organic synthesis, and for these reasons the reaction of ethyl diazoacetate with TESP was investigated. The possibility that the alkenylsodium salt 4 could deprotonate to liberate molecular nitrogen and afford an alkylidene carbene was especially intriguing.

The reaction of TESP (prepared in situ) with ethyl diazoacetate (3) under the same conditions which afford O-silylation with propanoate esters, gave an excellent yield (99%) of ethyl triethylsilyldiazoacetate (5). Silylated diazoacetates have been prepared previously by deprotonation of diazoacetates at low temperature followed by treatment of the resulting lithium derivatives with silyl chlorides, by metal exchange starting with mercury derivatives of ethyl diazooacetate, and through direct reaction of a chlorotrimethylsilane with the diazoester. The present convenient procedure affords higher yields than any previously known method.

Silylation of esters by triethylsilyl perchlorate in the presence of hindered tertiary amines is a very rapid and clean reaction. The substantially improved procedure reported here eliminates the need for isolation of the silyl perchlorate. We are currently exploring the possibility of replacing perchlorate derivatives in this procedure with other less hazardous leaving groups. Ongoing efforts in this laboratory are directed toward an exploration of the synthetic uses of the processes and products described herein.

1H-N.M.R. spectra were recorded on a Varian EM-390 (90 MHz) or Nicolet NT-200 (200 MHz) spectrometers. Chemical shifts are reported as values in parts per million relative to tetramethylsilane as internal standard. Capillary G.L.C. analysis was performed on a Varian 3700 instrument equipped with a 0.25 mm (I.D.) glass column, 25 m in length, wall coated with Carbowax 20M. Injection port temperatures (split ratio 400:1) were typically held at 200°C above the column oven temperature.

Dichloromethane, tetramethylguanidine, and disopropylmethylamine and isopropyl propanoate were distilled from calcium hydride immediately before use. Chloroform and chloroform-d were filtered through alumina (activity I) immediately prior to use. Triphenylmethyl perchlorate was prepared according to Dauben. Ethyl diazoacetate and triethylsilane (reagent grade commercial products) were used as obtained and without further purification. Dry ether was distilled from sodium metal in the presence of benzenophenone ketyl. Methanol was distilled from sodium.

(1) H-N.M.R. spectra were recorded on a Varian EM-390 (90 MHz) or Nicolet NT-200 (200 MHz) spectrometers. Chemical shifts are reported as values in parts per million relative to tetramethylsilane as internal standard. Capillary G.L.C. analysis was performed on a Varian 3700 instrument equipped with a 0.25 mm (I.D.) glass column, 25 m in length, wall coated with Carbowax 20M. Injection port temperatures (split ratio 400:1) were typically held at 200°C above the column oven temperature.
temperature in the dark, a clear, nearly colorless solution is obtained. To the mixture cooled again to ~ 78 °C, disisopropylaminoethylamine (4.85 g, 37.5 mmol) and then ethyl diazoacetate (3, 2.85 g, 25 mmol) is added dropwise over 3 min. After 15 min, the mixture is allowed to come to 0 °C and stirred for 15 min at 0 °C. The mixture is poured into pentane (500 ml), the pentane layer is washed with saturated sodium hydrogen carbonate solution (200 ml), water (2 × 200 ml), brine (100 ml) and dried with magnesium sulfate. Filtration and evaporation of volatile constituents affords a bright yellow semisolid. This is distilled through a 3.5 cm long Vigreux column to give a yellow liquid; yield: 5.86 g (~100%); b.p. 40–42 °C/0.05 torr. This is found to be a mixture of 97% of the desired product contaminated with 3% of hexaethylsiloxane. Further purification is achieved by column chromatography on silica gel (2.5 × 10 cm), eluting first with pentane (50 ml) and then with dichloromethane (200 ml). Evaporation of solvent from the second fraction affords the pure product; yield: 5.13 g (90%); b.p. 41–42 °C/0.05 torr; nD²⁰: 1.4691.

H.R.M.S.: calc. for C₃₁H₆₄N₂O₂Si: 228.1294; found: 228.1287.

I.R. (Film): ν = 2091, 1692, 1367, 1267 (br.), 1208, 1075, 1010 cm⁻¹.

U.V. (CH₃CN): λmax = 249 (ε = 10600); 372 nm (60)

H-N.M.R. (200 MHz, CDCl₃): δ = 0.75 (complex q, 6 H); 0.20 (complex t, 9 H); 1.26 (t, 3 H, J = 7.1 Hz); 4.19 ppm (q, 2 H, J = 7.1 Hz).

C-N.M.R. (CDCl₃): δ = 2.8 (t), 6.5 (q), 13.9 (q), 31.7 (s), 60.0 (t), 168.6 ppm (s).

Received: March 21, 1985


2 We have observed that equilibrating mixtures of propanoate derived silylketene acetas favor the (Z)-isomer: Wilcox, C.S., Babst, R.E. J. Org. Chem. 1984, 49, 1451.

3 More precisely, the major product from primary and secondary propanoates was observed to be identical with the minor product obtained by silylation of the enolate anion formed from those esters by the action of lithium disopropylamidite in tetrahydrofurran at ~ 78 °C. The major product derived from t-butyl propanoate using silyl perchlorates was identical with the major product obtained by lithium disopropylamidite deprotonation in tetrahydrofurran and subsequent silylation. Assignments were base on these comparisons and Ireland's work, which has established that the major silylketene acetal formed by lithium disopropylamidite/tetrahydrofurran deprotonation and silylation is of (E)-configuration.


6 This method was used by Barton and Tully in their original preparation of these compounds. An alternative procedure based on the reaction of silver perchlorate with silyl chlorides is in our opinion more dangerous due to the possibility that the product is more likely to retain inorganic perchlorate contaminants.

7 It has been shown that alkoxy- and halo-substituted alkyl diazonium salts are stable and readily isolated at room temperature:


