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ORIGINAL PAPER

Synthesis and some properties of silylated chitins as key intermediates for chemical modifications

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Abstract Triethylsilyl- and triphenylsilyl-chitins were synthesized from *β*-chitin in addition to trimethylsilyl-chitin, and the resulting three kinds of silylated chitins were evaluated in terms of solubility, stability, and reactivity as precursors for chemical modifications. Triethylsilylation was effected under appropriate conditions though less facilely than trimethylsilylation. Triphenylsilylation was sluggish, and full substitution appeared to be difficult. The silylated products were soluble in organic solvents unlike the starting chitin. Of the three derivatives, trimethylsilyl-chitin was the most soluble and reactive, but the least stable. Triethylsilyl-chitin would be a convenient intermediate for modifications because of the considerable reactivity and stability, and triphenylsilyl-chitin may be a useful protected derivative.

Keywords Chitin · Chemical modification · Triethylsilylation · Triphenylsilylation · Trimethylsilylation · Stability · Reactivity · Solubility

Introduction

Although chitin is an abundant amino polysaccharide easily accessible from food waste of crabs and shrimps, it has been discarded mostly. However, it is currently attracting much attention because of the distinctive biological activities in sharp contrast to the rather inert nature of cellulose, a glucan counterpart [1–4]. Chitin is thus considered a promising renewable biomaterial, but it is insoluble in solvents except some special ones such as hexafluoroacetone [5], *N*,*N*-dimethylacetamide/LiCl [6], and methanol/$CaCl_2$ [7] and is thus difficult to manipulate for fabrications and

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structural modifications. Such properties undoubtedly delayed its utilizations as well as basic studies despite the high potential in various fields as a specialty biopolymer.

Solubilization in common solvents should be a key to overcoming the intractable nature, and actually, incorporation of some proper substituents into chitin afforded soluble precursors, which have enabled efficient chemical modifications including a series of regioselective transformations of this multifunctional biopolymer to construct desirable molecular architectures [8–16]. Of various modifications, silylation is expected to be effective for both solubilization and protection depending on the structures of silyl groups, and we have reported the trimethylsilylation of chitin [17, 18]. Trimethylsilylated chitin showed exceptionally high solubility even in acetone and pyridine, and various chemical modifications became possible in solution efficiently and quantitatively. However, the derivative is very sensitive to humid, easily releasing the trimethylsilyl groups, and the freshly prepared product should be used for chemical modifications. Compared to the trimethylsilyl group, triethylsilyl and triphenylsilyl groups would be superior for enhancing stability of the products, and yet the silylated products would be organosoluble. In this article, we discuss the three types of silylation reactions and some characteristics of the resulting silylated derivatives to develop convenient precursors for chemical modifications of chitin.

Experimental

General

IR spectra were recorded on a Shimadzu FTIR-8900 instrument by the KBr method. ^{1}H NMR spectra were obtained with a JEOL JNM-LA400D in deuterated pyridine at ambient temperature at 400 MHz. Elemental analysis was performed on a Perkin Elmer 2400 II instrument. Solvents were purified in usual manners and stored over molecular sieves. 4-Dimethylaminopyridine (DMAP) was purified by recrystallization from ethyl acetate. Other chemicals were of reagent grade and used without further purification.

Chitin

β-Chitin was isolated from squid pens [19, 20], and the degree of deacetylation was 0.11 as determined by conductometric titration with a DKK TOA conductivity meter CM-20J [21, 22]. After pulverization to 0.5 mm mesh with an ultracentrifugal mill Retsch ZM-1, it was selectively *N*-acetylated with acetic anhydride in methanol according to the reported method [23]. Conductometric titration indicated that the product was fully *N*-acetylated. It was thoroughly dried with phosphorus pentoxide at 60 °C before use. IR (KBr): *ν* 3500–3200 (OH), 1655 (amide I), 1558 (amide II), and 1150–1000 cm^{-1} (pyranose).

Trimethylsilylation

The reaction of *β*-chitin with hexamethyldisilazane/chlorotrimethylsilane in pyridine was conducted in a manner reported elsewhere to give a fully substituted derivative, which was isolated as a white cotton-like fluffy material [18]. The degree of substitution (ds) for the silyl group was confirmed to be 2.0 by NMR and elemental analysis data.

Triethylsilylation

To a solution of 1.50 g of DMAP (12.35 mmol) in 25 mL of pyridine was added 0.50 g (2.47 mmol) of β-chitin. Chlorotriethylsilane (3.73 g, 24.7 mmol) was added, and the mixture was heated under reflux for 48 h with stirring in a nitrogen atmosphere. After cooling to room temperature, the mixture was poured to 300 mL of 50% aqueous methanol. The precipitate was collected by filtration, washed in 150 mL of methanol overnight, and dried to give a light brown solid. It was dissolved in 50 mL of pyridine and reprecipitated in 300 mL of water to give 0.94 g of the product as a white powdery material. The ds value determined by elemental analysis was 1.95, and the yield was 89%. IR (KBr): ν 3337 (NH and OH), 2955–2878 (CH), 1665 (amide I), 1528 (amide II), 1458 ($SiEt_3$), 1415 ($SiEt_3$), 1240 ($SiEt_3$), 1150–1000 (pyranose), 1016 ($SiEt_3$), 812 ($SiEt_3$), 740 ($SiEt_3$), and 731 cm^{-1} ($SiEt_3$). ^{1}H NMR (pyridine-d_5): δ 0.83 ($SiC\underline{H}_2CH_3$), 1.10 ($SiCH_2C\underline{H}_3$), 2.31 ($COCH_3$), and 3.7–4.5 ppm (pyranose).

Anal. Calcd for $(C_{20}H_{41}NO_5Si_2)_{0.95}(C_{14}H_{27}NO_5Si)_{0.05}\cdot 0.2H_2O$: C, 55.08; H, 9.55; N, 3.26. Found: C, 55.10; H, 9.55; N, 3.26.

Triphenylsilylation

A suspension of β-chitin (0.50 g, 2.47 mmol) in 50 mL of pyridine containing 0.84 g of imidazole (12.35 mmol) and 3.64 g (12.35 mmol) of chlorotriphenylsilane was heated at 100 °C for 48 h with stirring in nitrogen. The mixture was cooled to room temperature and poured to 300 mL of methanol. The precipitate was collected by filtration, washed with methanol, and dried to give 0.84 g of the product as a white powdery material. The ds was 1.66 as determined by elemental analysis: yield 89%. IR (KBr): ν 3412 (NH and OH), 3086–3007 (arom CH), 1680 (amide I), 1589 (phenyl), 1514 (amide II), 1429 ($SiPh_3$), 1150–1000 (pyranose), 1117 ($SiPh_3$), 743 ($SiPh_3$), 714 ($SiPh_3$), 700 ($SiPh_3$), and 509 cm^{-1} ($SiPh_3$).

Anal. Calcd for $(C_{44}H_{41}NO_5Si_2)_{0.66}(C_{26}H_{27}NO_5Si)_{0.34}\cdot 0.4H_2O$: C, 71.16; H, 5.84; N, 2.19. Found: C, 71.05; H, 5.66; N, 2.19.

IR calibration lines

Mixtures (1 mg) of trimethylsilyl-chitin of ds 2.00 and β-chitin of varying ratios were ground with 50 mg of potassium bromide. Disks were made from a small portion of the mixtures, dried thoroughly with phosphorus pentoxide at 60 °C, and subjected to IR spectroscopy. Absorbance ratios of two bands were calculated using the baselines drawn over 1780–950 cm^{-1} in the transmittance spectra and calibrated with ds values.

In a similar manner, absorbance ratios of two bands of triethylsilyl-chitins with various ds values were obtained with baselines over 1850–800 cm^{-1} and plotted against ds values.

Desilylation

A suspension of pulverized trimethylsilyl-chitin (ds 2.00, 0.200 g) in 50 mL of water, 50% aqueous methanol, 0.1 mol/L aqueous sodium hydroxide, or 0.1 mol/L aqueous acetic acid was stirred with a magnetic stirrer at 25 °C. A small amount of the suspension was pipetted after a certain time and filtered. The solid was washed with water and dried. The ds for trimethylsilyl group was determined using the IR calibration line.

Desilylation behavior of triethylsilyl-chitin with ds 1.89 was examined in the same manner, and the decrease in the ds was followed by the IR calibration line.

Acetylation of silylated chitins

To a solution of 0.066 g (ds 1.85, 0.144 mmol) of triethylsilyl-chitin and 0.018 g (0.144 mmol) of DMAP in 2 mL of pyridine was added 0.74 g (7.2 mmol) of acetic anhydride, and the mixture was stirred at room temperature for 24 h in a nitrogen atmosphere. The resulting solution was poured to 300 mL of water, and the precipitate was isolated by filtration, washed with 50 mL of acetone, and dried to give 0.043 g of the product as a white powdery material. The ds for acetyl was 1.38 calculated on the basis of the composition of the diacetylated unit and monoacetyl-monotriethylsilyl unit. IR (KBr): v 3410 (NH), 2957–2878 (CH), 1744 (ester C=O), 1663 (amide I), 1541 (amide II), 1150–1000 (pyranose), 816 ($SiEt_3$), and 745 cm^{-1} ($SiEt_3$).

Anal. Calcd for $(C_{12}H_{17}NO_7)_{0.38}(C_{16}H_{29}NO_6Si)_{0.62}$: C, 52.38; H, 7.42; N, 4.22. Found: C, 52.49; H, 7.59; N, 4.21.

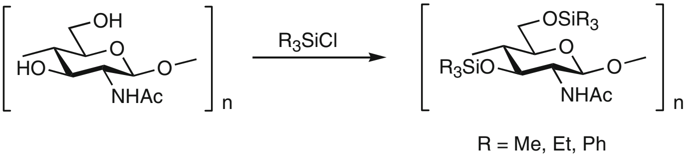
Acetylation of triphenylsilyl-chitin was carried out by the same method. In brief, starting from 0.100 g of triphenylsilyl-chitin of ds 1.73, 0.080 g of a white powdery acetylated product was obtained after 48 h reaction at room temperature in pyridine containing DMAP. The ds was calculated to be 0.29, provided that the product was composed of the monoacetyl-monotriphenylsilyl unit and ditriphenylsilyl unit. IR (KBr): v 3408 (NH), 3086–3007 (arom CH), 1746 (ester C=O), 1678 (amide I), 1589 (phenyl), 1516 (amide II), 1429 ($SiPh_3$), 1150–1000 (pyranose), 1117 ($SiPh_3$), 743 ($SiPh_3$), 714 ($SiPh_3$), 700 ($SiPh_3$), and 509 cm^{-1} ($SiPh_3$).

Anal. Calcd for $(C_{28}H_{29}NO_6Si)_{0.29}(C_{44}H_{41}NO_5Si_2)_{0.71}\cdot 0.4H_2O$: C, 71.15; H, 5.81; N, 2.11. Found: C, 71.17; H, 5.64; N, 2.11.

Results and discussion

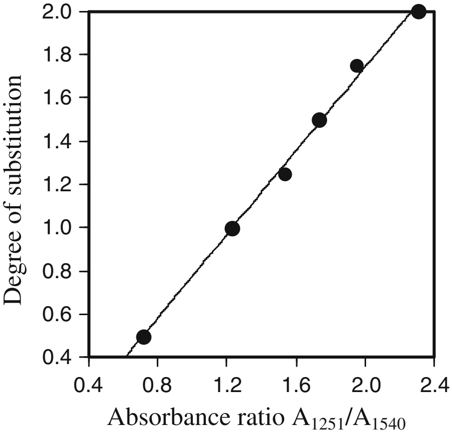
Silylation

Because of the weaker intermolecular forces, β-chitin is more susceptible to modification reactions including acetylation, triphenylmethylation [23], and trimethylsilylation [18] than the ordinary α-chitin. Fully *N*-acetylated β-chitin [23] was thus used as a structurally uniform starting material to synthesize silylated derivatives with well-defined structures (Scheme 1).



Scheme 1 Silylation of chitin

Fig. 1 Calibration line for determining the ds for trimethylsilyl



Trimethylsilylation

Trimethylsilylation of chitin was performed according to the reported method [18], and a fully substituted derivative (ds 2.00) was prepared. To determine the ds in a simple manner, relationships between the ds and absorbance ratios of IR absorption bands at around 1664 (amide I), 1540 (amide II), 1251 (silyl), and 842 cm^{-1} (silyl) were plotted against the ds values, and the ratio A_{1251}/A_{1540} was found to show better linearity than the others (Fig. 1).

Triethylsilylation

The reaction was carried out with chlorotriethylsilane in pyridine, but was slow compared with trimethylsilylation using a mixture of chlorotrimethylsilane and hexamethyldisilazane. Substitution behavior is shown in Fig. 2, and DMAP proved effective to facilitate the substitution. Almost full substitution (ds 1.95) was achieved by the reaction under reflux for 48 h. The crude products assumed a brown color, but reprecipitation afforded colorless powdery materials. The yields were generally satisfactory in the range of 80–90%. Figure 3B shows the IR spectrum of triethylsilylated chitin, and the introduction of triethylsilyl groups was apparent by characteristic absorption bands at 2955–2878 cm^{-1} for ethyl, and those at around 1458, 1415, 1240, 1016, 812, 740, and 731 cm^{-1} for triethylsilyl. The ^1H NMR spectrum in Fig. 4 supported the structure, showing peaks at 0.83 and 1.10 ppm due to triethylsilyl and that at 2.31 ppm due to *N*-acetyl.

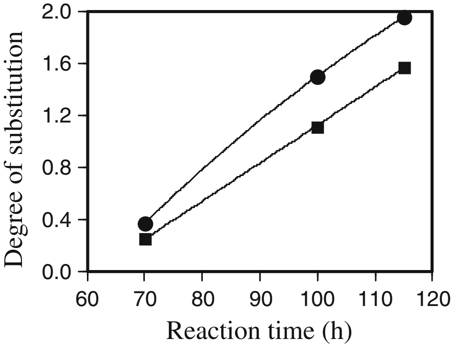


Fig. 2 Triethylsilylation with (*filled circle*) or without (*filled square*) DMAP

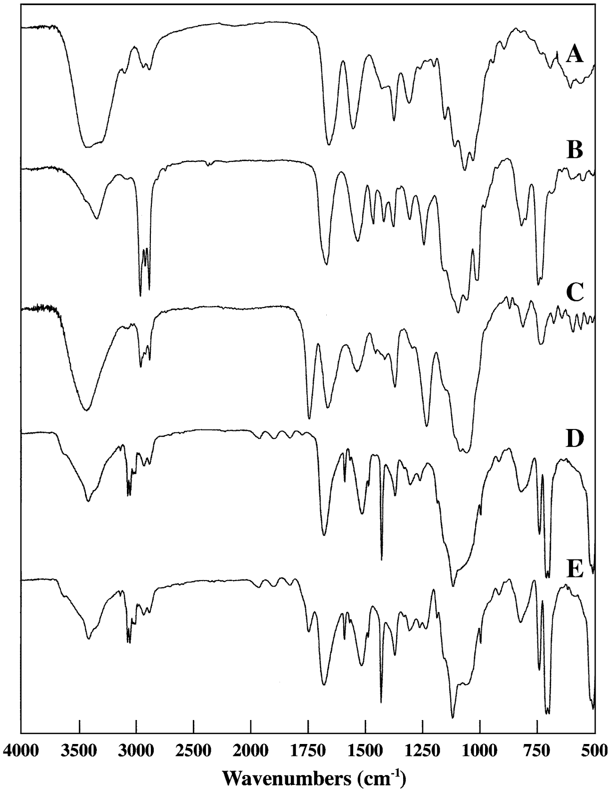


Fig. 3 IR spectra of chitin and the derivatives (KBr method): *A* β-chitin; *B* triethylsilyl-chitin (ds 1.95); *C* acetylated triethylsilyl-chitin (ds for acetyl, 1.38); *D* triphenylsilyl-chitin (ds 1.73); *E* acetylated triphenylsilyl-chitin (ds for acetyl, 0.29)

To determine the ds value in a simple manner, the ratios of absorbances at 1460, 1240, and 744 cm^{-1} to those of amide I and II bands were plotted against the ds values. Of various possible combinations, A_{1240}/A_{1531} appeared to be superior to the others in terms of linearity (Fig. 5).

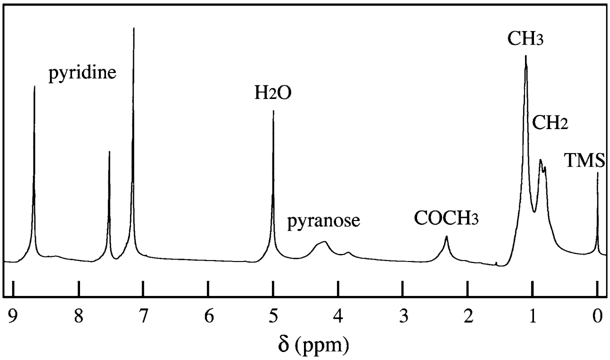
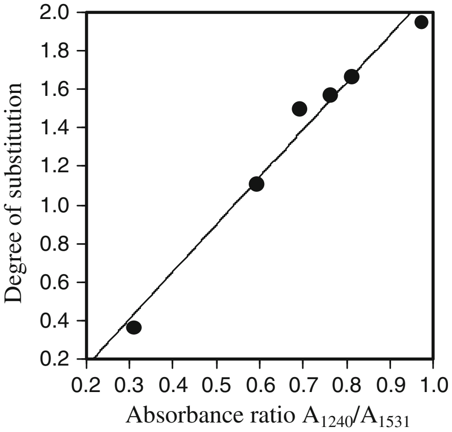


Fig. 4 ^{1}H NMR spectrum of triethylsilyl-chitin (ds 1.87) in deuterated pyridine

Fig. 5 Calibration line for determining the ds for triethylsilyl



Triphenylsilylation

The triphenylsilyl group is rather bulky, and the substitution was obviously sluggish compared with trimethylsilylation and triethylsilylation. The reaction with chlorotriphenylsilane was first attempted in the presence of DMAP, but the ds values of the products were low. As a reaction promoter, imidazole was found more suitable, and the ds of the resulting triphenylsilyl-chitin was 1.73 under reflux and 1.66 at 100 °C after 48 h reaction. Figure 3D shows bands due to aromatic C–H and triphenylsilyl groups.

Solubility

Qualitative solubility test was done with a 0.5 mg sample in 0.75 mL of solvent, and the results are summarized in Table 1. Trimethylsilyl-chitin exhibited remarkable solubility in common solvents. Triethylsilyl- and triphenylsilyl-chitins also showed highly improved solubility compared with the original chitin; they were

Table 1 Solubility of chitin and the silylated derivatives

	Pyridine	DMSO	DMF	Acetone
Chitin	–	–	–	–
Trimethylsilyl-chitin (ds 2.00)	++	+	±	++
Triethylsilyl-chitin (ds 1.95)	+	±	±	±
Triphenylsilyl-chitin (ds 1.73)	++	±	±	±

DMSO dimethyl sulfoxide; *DMF N,N*-dimethylformamide; ++ soluble at rt; + soluble on heating; ± partially soluble or swelled; – insoluble

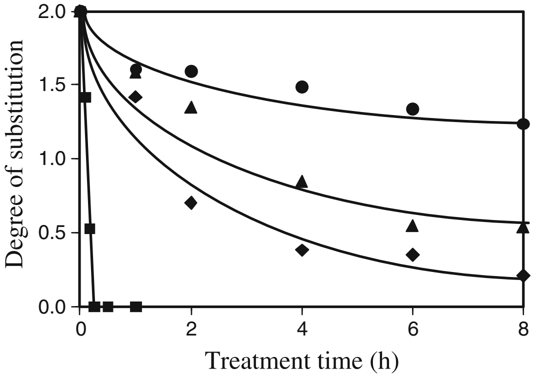


Fig. 6 Detrimethylsilylation in water (*filled circle*), 50% aqueous methanol (*filled triangle*), 0.1 mol/L sodium hydroxide (*filled diamond*), and 0.1 mol/L acetic acid (*filled square*) at 25 °C

readily soluble in pyridine and highly swelled in dimethyl sulfoxide, *N*,*N*-dimethylformamide, and acetone.

Desilylation

To evaluate the stability or deprotection manner of silylated chitins, pulverized trimethylsilyl- and triethylsilyl-chitins were treated with water, 50% aqueous methanol, 0.1 mol/L sodium hydroxide, and 0.1 mol/L acetic acid at 25 °C.

The trimethylsilyl ether linkage is quite labile under acidic conditions, and the ds dropped to zero in 15 min in aqueous acetic acid, indicating that the trimethylsilyl group can be thoroughly removed with aqueous acetic acid in a short time under mild conditions (Fig. 6). In water, aqueous methanol, and aqueous sodium hydroxide, however, desilylation proceeded less rapidly, and the ds values were 1.24, 0.54, and 0.21, respectively, after 8 h treatment.

In sharp contrast to trimethylsilyl-chitin, triethylsilyl-chitin was considerably stable in these solvents as evident in Fig. 7, and no appreciable reduction in ds was detected in 24 h in both water and aqueous methanol. Even in aqueous sodium hydroxide and acetic acid, the ds decreased only slightly from 1.89 to 1.86 and 1.82.

Detriethylsilylation was thus confirmed rather resistant and then examined at elevated temperatures in 0.1 mol/L sodium hydroxide and acetic acid. Even after treatment in aqueous sodium hydroxide at 60 °C for 24 h, weak absorption bands due to triethylsilyl were observed in the IR spectra. Although the reaction was much

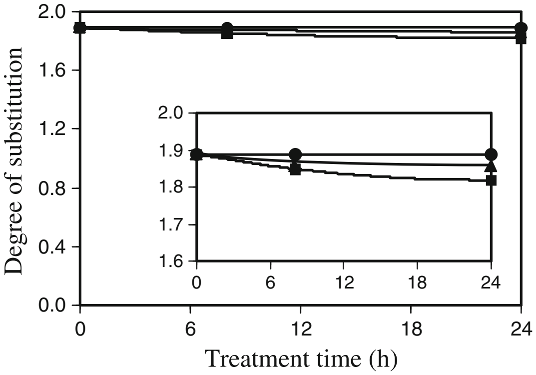


Fig. 7 Detriethylsilylation in water and 50% aqueous methanol (*filled circle*), 0.1 mol/L sodium hydroxide (*filled triangle*), and 0.1 mol/L acetic acid (filled square) at 25 °C

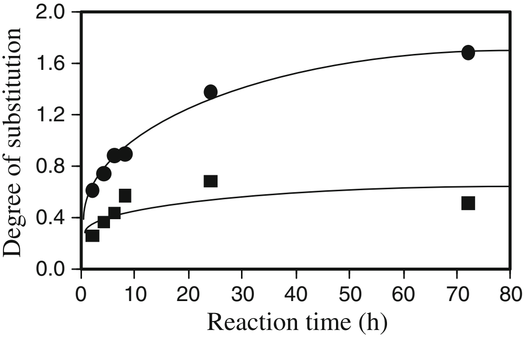


Fig. 8 Acetylation of triethylsilyl-chitin (ds 1.85) with (*filled circle*) or without (*filled square*) DMAP

more facile in aqueous acetic acid, a small amount of triethylsilyl groups still remained after 24 h at 40 or 50 °C as suggested by IR spectroscopy. However, complete detriethylsilylation could be attained in 24 h at 60 °C.

Acetylation

Trimethylsilyl-chitin has proved a versatile precursor for chemical modifications owing to its high solubility in common organic solvents and improved reactivity in solution. It was actually confirmed to be a useful starting material for structural modifications such as acetylation and triphenylmethylation [18].

To elucidate the reactivity of triethylsilyl-chitin, acetylation was conducted at room temperature in pyridine in the presence or absence of DMAP. The products were isolated in water, but the IR spectra indicated the presence of significant amounts of silyl groups in addition to *O*-acetyl groups as apparent in Fig. 3C. The extent of reaction was thus calculated from the elemental analysis data, provided that every hydroxyl group carried either an acetyl or triethylsilyl group. As shown in Fig. 8, DMAP effectively facilitated the reaction, and the ds for acetyl reached 1.69 after 72 h, indicating that triethylsilyl groups could be largely replaced with acetyl groups under these conditions. The substitution was also evidenced by the markedly weakened bands characteristic of aliphatic C–H and triethylsilyl in the IR spectrum.

Triphenylsilyl-chitin was acetylated only to a low extent as expected, and the ds for acetyl remained around 0.3 even in the reaction for a prolonged time in the presence of DMAP. This implies that the triphenylsilyl ether linkage is stable and triphenylsilyl is not replaced with acetyl. This is also supported by the IR spectrum of the acetylated product (Fig. 3E).

Conclusions

Although triethylsilylation gave rise to an almost fully substituted chitin derivative under appropriate conditions, reaction was less facile than trimethylsilylation. Triphenylsilylation was even more sluggish, and it was difficult to attain full substitution. The resulting three kinds of silylated chitins were soluble in common organic solvents such as pyridine. Compared to trimethylsilyl-chitin that is a highly reactive organosoluble precursor for various modification reactions, triethylsilyl-chitin exhibited moderate reactivity in acetylation, and silyl groups could be replaced with acetyl groups under mild conditions. Triphenylsilyl groups were found difficult to substitute, and only the free hydroxyl groups were acetylated under ordinary conditions. Therefore, trimethylsilyl is favorable for enhancing reactivity as well as solubility, but the silyl ether linkage is rather unstable. Triphenylsilyl plays a role as a protective group, and triethylsilyl can enhance reactivity or protect the hydroxyl group depending on the reaction conditions. Consequently, a proper choice of silyl groups would make possible formation of derivatives with desirable properties suitable for controlled chemical modifications to construct well-defined molecular environments based on chitin.

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