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New biosurfactants based on germylated fatty compounds

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A simple and efficient method for producing amphiphilic germylated compounds has been developed by hydrogermylation of fatty acid methyl esters. The germylated precursors afford a micelle-type assembly in various solvents as evident by the formation of nano-objects, micrometer spheres and lamellar forms. This offers a promising route to synthetically useful monomers for structured materials.

Keywords: fatty acid esters; hydrogermylation; radical initiation; self-assembly

Introduction

Over the last 30 years, the design of new molecular assemblies has been intensively pursued, not only for their fundamental scientific interest, but also for their many technological applications.[1–4] Nanomaterials exhibit very interesting size-dependent electrical, optical, magnetic and chemical properties that cannot be achieved by their bulky counterparts.[5] In this context, intensive efforts have been made to synthesize structured hybrid materials by using surfactant assemblies as structure initiators. The formation of such materials is governed by weak interactions between surfactant molecules and inorganic species.[6–8] The control of hybrid nanostructures without the use of surfactants is a great challenge, and the preparation of novel building blocks with self-organizing ability is important because the design of each new precursor opens a possible way to form nanohybrid materials that are not accessible by surfactant directed processes. In this regard, structured materials based on alkylsulfates and alkylpyridinium halides are relatively toxic, and, as such, cannot be used directly in drug carrier formulations.[9–11] Therefore, it will be advantageous to design novel assembled systems with a natural surfactant as one of the components. Recently, we initiated a research program aimed at investigating various aspects of silylation of oleochemical compounds in order to obtain hydrophilic and/or hydrophobic biocompatible polysiloxanes.[12–15] Besides their ready availability, biodegradability and important properties of biocompatibility, fatty compounds exhibit unique properties of self-organization.[16] As part of our continuing research program to develop novel extended structures based on oil-type compounds, we have investigated the reactivity of unsaturated fatty compounds (fatty acid methyl esters, FAME) toward germanium hydrides. To the best of our knowledge, the hydrogermylation of unsaturated natural fats has never been investigated and remains a stimulating challenge. Such amphiphilic germylated precursors should be very interesting in nanomaterials, biomedical applications and material science as they present a heavy group 14 element with generally low toxicity. In this communication, we report the facile synthesis of new dentritic germylated fatty compounds as amphiphilic biomacromolecules and their structures in various solvents.

Results and Discussion

Hydrogermylation of methyl 10-undecenoate

Hydrogermylation is a term describing the addition of germanium hydrides to carbon–carbon or carbon–heteroatom multiple bonds.[17] Radical initiators and transition metal catalysts are well known to be effective in accelerating hydrometalations.[18] Although hydrogermylation of alkenes, carbonyls and α,β-unsaturated carbonyl compounds have been reported, there are no reports of hydrogermylation of unsaturated FAME. In order to optimize the reaction conditions, we first investigated the hydrogermylation of methyl 10-undecenoate with triphenylgermane (Scheme 1).

The reaction was monitored by ^{1}H NMR spectroscopy. Thermally induced hydrogermylation of methyl 10-undecenoate was highly favoured, leading to 72% hydrometalation. The use of AIBN as an initiator was required to achieve complete the consumption of the starting olefin. The germylated product (methyl 11-triphenylgermylundecanoate) **1** was isolated in 93% yield by distillation. It is thermally stable, easy to handle, perfectly storable and is not sensitive to moisture. Spectroscopic data indicated that germanium hydride had added to the C=C bond without interaction between the germanium center and the carbonyl group. The reaction is regiospecific and only the anti-Markovnikov product was obtained because no ^{13}C NMR signal corresponding to CH_3-$CH(GePh_3)$-CH_2 was observed.

We then investigated the reactivity of methyl 10-undecenoate with diphenylgermane Ph_2GeH_2 and phenylgermane $PhGeH_3$ (Schemes 2–4). Starting from Ph_2GeH_2, we performed selectively mono- and di-hydrogermylations. One equivalent of methyl

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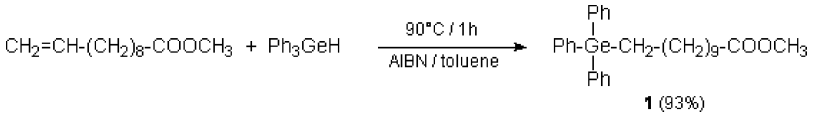
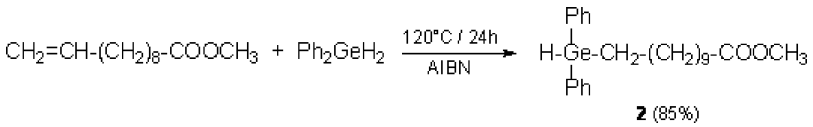
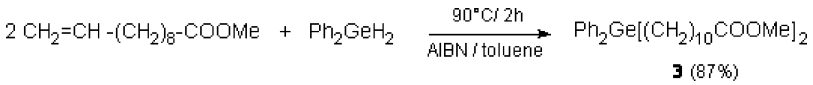


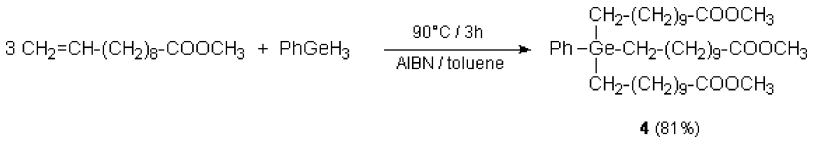
Scheme 1. Regioselective hydrogermylation of methyl 10-undecenoate.



Scheme 2. Regioselective monohydrogermylation of methyl 10-undecenoate.



Scheme 3. Regioselective dihydrogermylation of methyl 10-undecenoate.



Scheme 4. Regioselective trihydrogermylation of methyl 10-undecenoate.

10-undecenoate and Ph_2GeH_2 under AIBN at 120 °C led selectively to the monohydrogermylated product **2**.

Compound **2** was isolated by distillation in 85% yield. It exhibits NMR characteristics very similar to those of **1** with additional signals assigned to the remaining Ge-H bond. In ^{1}H NMR, the proton linked to germanium was observed at 5.11 ppm (t, $J = 3.2$ *Hz*), and in infrared spectroscopy, the Ge-H vibration was located at 2030 cm^{-1}. Starting with 2 equivalents of methyl 10-undecenoate, **3** was selectively obtained in 87% yield.

Compound **3** was isolated as a pure liquid in 87% yield by distillation. All the spectroscopic data confirmed the proposed composition. The reactivity of $PhGeH_3$ toward unsaturated fatty compounds was also investigated to test the scope and limitation of the proposed strategy (Scheme 4). This germane added easily to 3 equivalents of methyl 10-undecenoate to give the germylated triester **4**. Interestingly, 3 h heating at 90 °C in the presence of AIBN as an initiator were enough to achieve complete hydrometalation. Compound **4** was isolated as a liquid in 81% yield after distillation, and was perfectly characterized. However, care had to be taken because it decomposes slightly at 180 °C/0.2 mmHg.

Self-assembly of germylated fatty compounds

The amphiphilic character of the germylated precursors described here makes them very attractive for material applications, especially as new building blocks for the rational design of hybrid materials. Thus, it was interesting to know whether these precursors would be capable of forming solvent-dependent micelle-type assemblies. The simple dissolution of our samples in various solvents might give an idea about their ability to self-assemble. Accordingly, three solutions of each precursor were prepared in dimethylsulfoxide (DMSO), water and heptane. After stirring for 15 min, each solution was deposited on a grid of carbon and then analyzed by transmission electronic microscopy (TEM). The description of the observed species (morphologies and size) is given in Table 1.

TEM images obtained from these solutions are shown in Figs 1–4, which suggest that these precursors afford micelle-type assemblies as evident by the formation of nanoparticles. The variety of the morphologies obtained reflects the effect of the solvent during the structure-forming process. For instance, in dimethylsulfoxide, germylated polyesters **3** and **4** led to highly uniform spherical species, 2.5–4 and 3 μm respectively. In heptane however, uniform-sized monodisperse nanoparticles (2 and 10 nm) were obtained under mild conditions. Hydrocarbon solvents have been used extensively in the synthesis of monodisperse nanocrystals of metals by thermal decomposition of metal/oleate complexes.[19,20] In fact, methyl oleate can play a role as a stabilizer, controlling the growth of inorganic oxide and, by a cooperative effect with a non-polar solvent, prevents the agglomeration of nanospecies and consequently leads to homogenous and dispersed nanoparticles. In water, TEM images of diester **3** and triester **4** confirmed layered structures by showing some well-ordered features with lamellar spacings (interlayer distances about 2 nm). This organization appeared to be dependent on the hydrophobic properties of the long chain spacer in germylated precursors. The use of alkyltrialkoxysilane having a long alkyl chain has led to layer-ordered hybrid materials.[21–25] The solvent seems to play a crucial role. As reported by Moreau *et al*. in the preparation of lamellar-bridged silsesquioxanes by self-assembly of hydrophobic long chains, lamellar organization was obtained exclusively with excess water, whereas with ethanol amorphous solids resulted.[26] It is noteworthy that no organisation or self-assembly in the nanoscale domain was observed by dissolution of methyl oleate or methyl undecenoate in dimethylsulfoxide, water or heptane. Similarly, some organic diesters did not show any interesting ability to assemble. In addition to the dependency of the shape and morphology of the resulting materials on the nature of solvents, aryl groups linked to germanium may induce supplementary ability to self-assemble. In fact, the choice of aryl groups is not irrelevant

Table 1. Morphologies and size of species formed by dissolution of the germylated precursors in solvents

Precursor	DMSO	H_2O	Heptane
3	Sphere of 2.5–4 μm	Lamellar organization	Nanoparticles (2 nm)
4	Sphere of 3 μm	Lamellar organization	Nanoparticules (10 nm)

$[C] = 3.5 \times 10^{-8}$ mol l^{-1}.

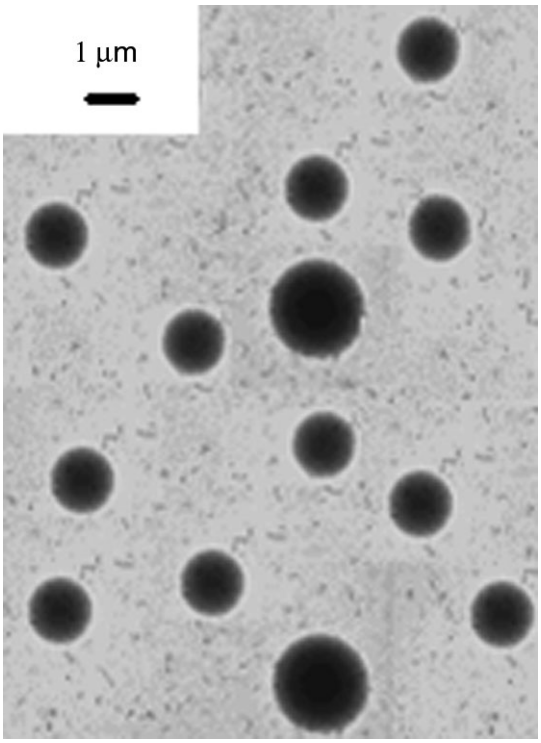


Figure 1. TEM image of 3 in DMSO.

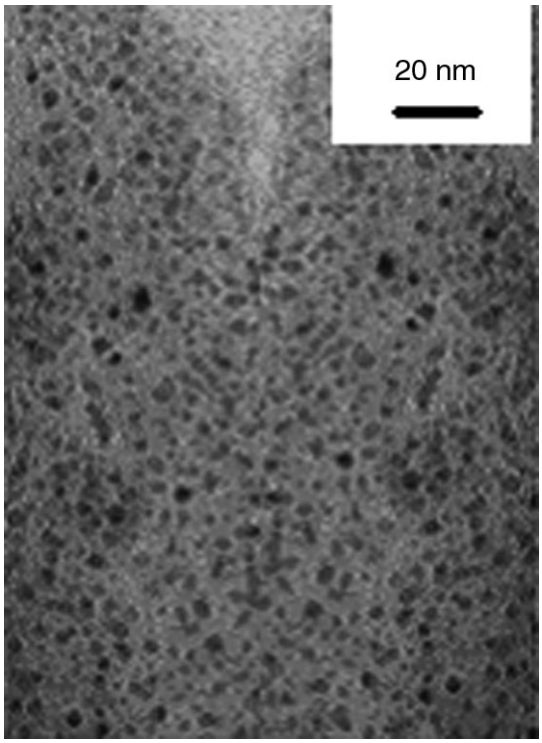


Figure 2. TEM image of 3 in heptanes.

because the $\pi - \pi$ stacking effect is known to be involved in the approaches to hierarchically dimensioned materials.[27–29]

Our preliminary results of the ability of germylated fatty compounds to self-assemble in certain solvents to produce small particles are so promising that additional studies are underway on a wider range of fatty compounds and solvents to better understand the processes involved.

Conclusions

In summary, the first synthesis and characterization of new oil-type compounds formed by hydrogermylation of methyl 10-undecenoate are reported. Owing to the low polarity of the aryl Ge–H bond, a radical initiation pathway using AIBN is very adaptable to arylgermanes as an alternative to metal catalysis. Hydrogermylation of ethylenic fatty acid derivatives by arylgermanes occurred easily in the case of terminal double bonds, allowing the preparation of germylated mono-, di- and tri-esters, interesting monomers for the design of new hybrid materials and biodegradable polyesters. The observed well-defined structures from germylated fatty compounds might provide a strategy to achieve nanostructured materials with biomimetic functions or drug delivery applications.

Experimental

All reactions were carried out under argon atmosphere using standard Schlenk tube techniques, and Carius tubes. Solvents were dried and distilled according standard procedures. Methyl 10-undecenoate was purchased from Aldrich and used without supplementary purification. Phenylgermanes were prepared according to literature procedures.[18] AIBN (azo bis-isobutyronitrile: $[Me_2C(CN)–N{=})_2$ was used in 1% concentration relative to organic reagents. NMR spectra were recorded in $CDCl_3$ at 20 °C on Bruker Avance 300 (^{1}H, 300.13 MHz) and Avance 300 (^{13}C, 75.48 MHz) spectrometers. Mass spectra were recorded with a Hewlett-Packard HP 5989 instrument in the electron impact mode (Ei, 70 eV). Infrared spectra were recorded on a Perkin Elmer 1600 FT spectrometer. Elemental analyses were carried out at the Centre de Microanalyses de l'Ecole Nationale Supérieure de Chimie de Toulouse. TEM images were obtained using a Jeol 1200EX II (120 kV).

Preparation of (Ph_3Ge)-CH_2-$(CH_2)_8$-CH_2-$COOCH_3$ (1)

A mixture of methyl 10-undecenoate (1.90 g, 9.59 mmol), triphenylgermane (3.50 g, 11.50 mmol) and AIBN in toluene (3 ml) was heated at 90 °C for 1h. The reaction was almost quantitative

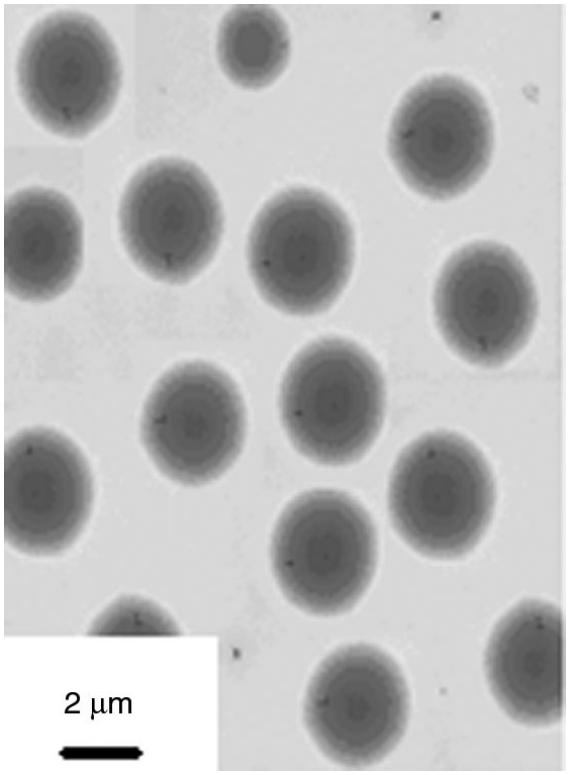


Figure 3. TEM image of 4 in DMSO.

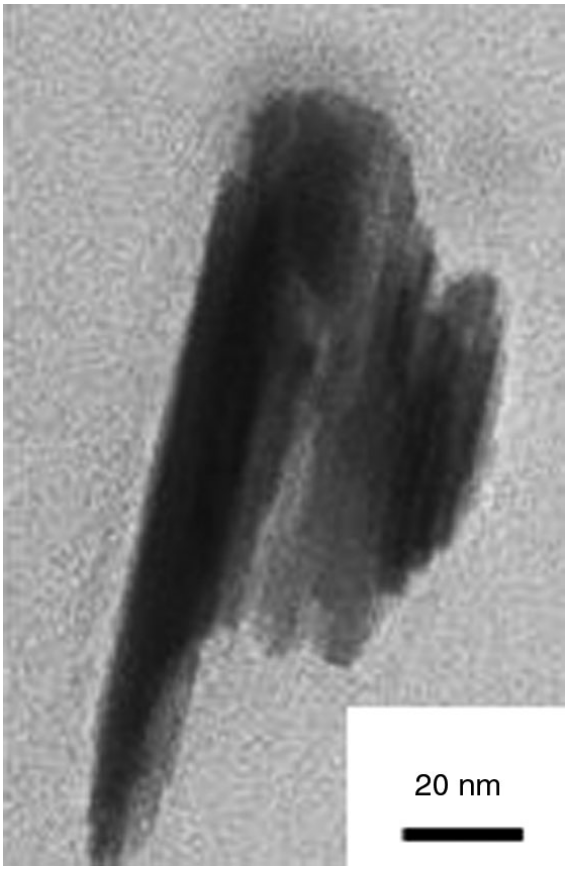


Figure 4. TEM image of 4 in water.

(100% by ^{1}H NMR analysis). Distillation under reduced pressure gave **1**. Yield: 4.49 g (93%). b.p., 138 °C/0.08 mmHg. ^{1}H NMR (300.13 MHz, $CDCl_3$, 20 °C): 1.14–1.55 [m, 18H, CH_2-(CH_2)$_8$]; 2.22 (t, $^3J_{HH}$ = 7.0 Hz, 2H, CH_2-CO); 3.59 (s, 3H, OCH_3); 7.27–7.40 (m, 15H, C_6H_5) ppm. ^{13}C NMR (75.48 MHz, $CDCl_3$, 20 °C): 14.04 (CH_2-Ge); 24.99, 25.05, 29.11, 29.18, 29.26, 29.44, 29.51, 33.48, [(CH_2)$_8$]; 34.19 (CH_2-CO); 51.56 (OCH_3); 127.86 (C_m); 128.54 (C_p); 135.01 (C_o); 135.32 (C_{ipso}), 174.42 (CO) ppm. IR (pure): ν = 1738 (C=O) cm^{-1}. MS (Ei): m/z = 504 [M + 1]$^+$, 473 [M − OCH_3 + 1]$^+$, 427 [M − Ph + 1]$^+$, 305 [Ph_3Ge]$^+$. Anal. found, C 71.22, H 7.15; calcd for $C_{30}H_{38}GeO_2$: C 71.60, H 7.61.

Preparation of (Ph_2HGe)-CH_2-(CH_2)$_7$-CH_2-CH_2-$COOCH_3$ (2)

A mixture of methyl 10-undecenoate (2.00 g, 10.10 mmol), diphenylgermane (2.78 g, 12.12 mmol) and AIBN was heated at 120 °C for 24 h. Distillation led to **3**. Yield: 3.67 g (85%). b.p., 116 °C/0.08 mmHg. ^{1}H NMR (300.13 MHz, $CDCl_3$, 20 °C): 1.43 [s.l, 18H, Ge-CH_2-(CH_2)$_7$$CH_2$]; 2.36 (t, $^3J_{HH}$ = 7.4 Hz, 2H, CH_2-CO); 3.71 (s, 3H, OCH_3); 5.11 (t, $^3J_{HH}$ = 3.2 Hz, 1H, GeHPh$_2$); 7.40–7.56 (m, 10H, C_6H_5) ppm. ^{13}C NMR (75.48 MHz, $CDCl_3$, 20 °C): 13.57 (CH_2-Ge); 25.10, 25.95, 29.30, 29.60, [(CH_2)$_7$]; 33.04 (CH_2-CH_2-CO); 34.22 (CH_2-CO); 51.55 (OCH_3); 128.12 (C_m); 128.57 (C_p); 135.09 (C_o); 137.07 (C_{ipso}), 174.40 (CO) ppm. IR (pure): ν = 1740 (C=O), 2030 (Ge-H) cm^{-1}. MS (Ei) m/z = 428 [M]$^+$, 397 [M − OCH_3]$^+$, 351 [M − Ph]$^+$, 228 [Ph_2Ge]$^+$. Anal. found, C 68.14, H 8.22; calcd for $C_{24}H_{34}GeO_2$: C 67.49, H 8.02.

Preparation of (Ph_2Ge)-[CH_2-(CH_2)$_7$-CH_2-CH_2-$COOCH_3$]$_2$ (3)

A mixture of two equivalents of methyl 10-undecenoate (1.70 g, 8.58 mmol) and diphenylgermane (1.83 g, 4.29 mmol) in toluene (3 ml) was heated at 90 °C for 2 h. Distillation led to 1.38 g of **3**. Yield: 87%. B.p.: 245 °C/0.03 mmHg. ^{1}H NMR (300.13 MHz, $CDCl_3$, 20 °C): 1.16 [s.l, 28H, Ge-CH_2-(CH_2)$_7$]; 1.32–1.35 (m, 4H, CH_2-Ge); 1.50–1.54 (m, 4H, CH_2-CH_2-CO); 2.21 (t, $^3J_{HH}$ = 6.6 Hz, 4H, CH_2-CO); 3.57 (s, 6H, OCH_3); 7.24–7.38 (m, 10H, C_6H_5) ppm. ^{13}C NMR (75.48 MHz, $CDCl_3$, 20 °C): 13.32 (CH_2-Ge); 25.03, 25.54, 27.58, 29.24, 29.33, 29.53, 29.58 [(CH_2)$_7$]; 32.65 (CH_2-CH_2-CO); 34.14 (CH_2-CO); 51.49 (OCH_3); 128.41 (C_m); 128.51 (C_p); 134.50 (C_o); 138.87 (C_{ipso}), 174.30 (CO) ppm. IR (pure): ν = 1740 (C–O) cm^{-1}. MS (Ei) m/z: 626 [M]$^+$, 595 [M − OCH_3]$^+$, 549 [M − Ph]$^+$, 427 [M − (CH_2)$_{10}$ − $COOCH_3$]$^+$, 229 [Ph_2Ge + 1]$^+$, 151 [PhGe]$^+$. Anal. found: C, 69.40; H, 9.36; Calcd for $C_{36}H_{56}GeO_4$: C, 69.14; H, 9.02.

Preparation of (PhGe)-[CH_2-(CH_2)$_7$-CH_2-CH_2-$COOCH_3$]$_3$ (4)

A solution of methyl 10-undecenoate (2.00 g, 10.10 mmol) and $PhGeH_3$ (0.52 g, 3.38 mmol) and AIBN in toluene (2 ml) was heated at 90 °C. After 3 h, evaporation of solvent and distillation under reduced pressure led to triester **4**. Yield: 2.05 g (81%). b.p.: 260 °C/0.1 mmHg. ^{1}H NMR (300.13 MHz, $CDCl_3$, 20 °C): 0.88 (t, $^3J_{HH}$ = 6.0 Hz, 6H, CH_2-Ge); 1.18 [s.l, 42H, (CH_2)$_7$]; 1.49–1.56 (m, 6H, CH_2-CH_2-CO); 2.23 (t, $^3J_{HH}$ = 7.5 Hz, 6H, CH_2-CO); 3.59 (s, 9H, OCH_3); 7.23–7.36 (m, 5H, C_6H_5) ppm. ^{13}C NMR (75.48 MHz, $CDCl_3$, 20 °C): 12.96 (CH_2-Ge); 24.97, 25.10, 29.18, 29.21, 29.27, 29.48, 29.55 [(CH_2)$_7$]; 33.56 (CH_2-CH_2-CO); 34.11 (CH_2-CO); 51.41 (OCH_3); 127.78 (C_m); 127.99 (C_p); 133.85 (C_o); 140.68 (C_{ipso}), 174.29 (CO) ppm. IR (pure): ν = 1744 (C=O) cm^{-1}. MS (Ei) m/z: 717 [M − OCH_3]$^+$, 671 [M − Ph]$^+$, 549 [M − (CH_2)$_{10}$-$COOCH_3$]$^+$, 351 [PhGe-(CH_2)$_{10}$-$COOCH_3$ + 1]$^+$, 151 [PhGe]$^+$. Anal. found, C 66.74, H 9.94; calcd for $C_{42}H_{74}GeO_6$: C 67.47, H 9.98.

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