Use of Phenylselenyl Chloride in the Preparation of Methyl 11-Phenylseleno-10-acetamido- and Ethyl Phenylselenoethoxy Fatty Alkanoates

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ABSTRACT: Reaction of methyl 10-undecenoate (**I**) with phenylselenyl chloride in acetonitrile furnished methyl 11-phenylseleno-10-acetamido-undecanoate (**II**) as a major product, and a similar reaction of **I** with phenylselenyl chloride in absolute ethanol gave ethyl 11-phenylseleno-10-ethoxy-undecanoate (**III**) as a sole product. A similar reaction of methyl octadec-*cis*-9-enoate (**IV**; oleate) with phenylselenyl chloride in absolute ethanol was conducted and resulted in the formation of ethyl 10(9)-phenylseleno-9(10)-ethoxy-octadecanoate (**V**).

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KEY WORDS: Acetonitrile, addition products, ethanol, methyl 10-undecenoate, methyl octadec-*cis*-9-enoate, IR, MS, NMR, phenylselenyl chloride.

A literature survey revealed that phenylselenyl reagents participate in a number of useful reactions such as addition (1–4), cyclization (5–7), and others (8–10). These phenylselenyl reagents also are used in a number of reactions involving unsaturated compounds (11–13) to form aminoselenides and alkanones and for the effective introduction of unsaturated functionality (14,15). Thus, organoselenium compounds are useful as synthetic reagents. Recently, the biological activities of some organoselenium compounds were reported (16).

Although a large number of reactions using phenylselenyl chloride have been reported, very little work has been done on FA (17,18). In this work, we studied the addition reactions of methyl 10-undecenoate (**I**; Schemes 1,2) and octadec-*cis*-9-enoate (**IV**; Scheme 3) by using phenylselenyl chloride in acetonitrile or ethanol to give addition products.

EXPERIMENTAL PROCEDURES

IR spectra were obtained with a Shimadzu 8201 PC spectrophotometer as neat films. NMR spectra were recorded in $CDCl_3$ with a Bruker DRX 300 spectrometer. Chemical shifts were measured in ppm, downfield from the internal standard tetramethylsilane (δ = 0 ppm). Mass spectra (MS) were recorded on a Jeol D-300 (EI) mass spectrometer. The abbreviations *s, m, t, q*, and *br* stand for singlet, multiplet, triplet, quartet, and broad, respectively. Major diagnostic fragments in MS are shown in Figures 2, 4, and 5.

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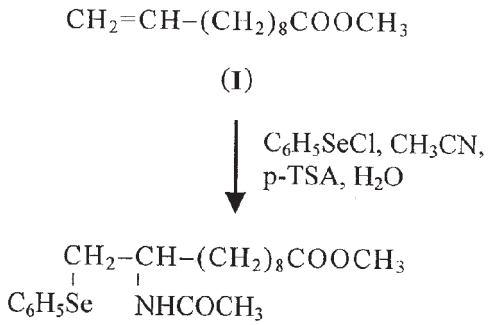
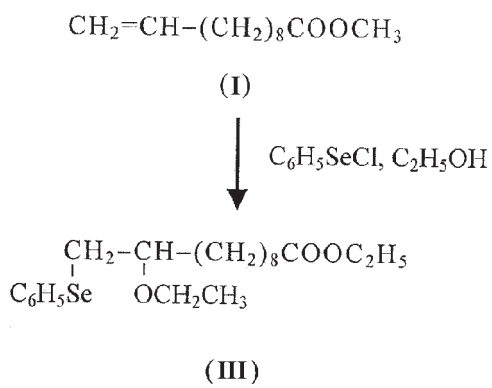
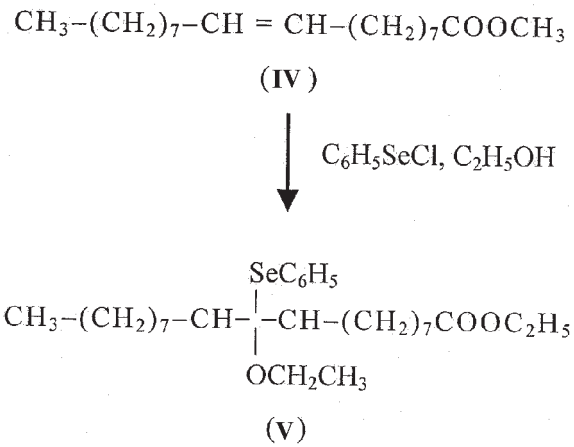


SCHEME 1



SCHEME 2



SCHEME 3

TLC plates (20 × 5 cm) were prepared in the laboratory and were coated with a layer of silica gel G (0.25 mm thickness; Merck, Mumbai, India) and a mixture of petroleum ether/diethyl ether/acetic acid (80:20:1, by vol) was normally used as the developing solvent. Compounds on the TLC plates were visualized by charring the sprayed plates with a 20% aqueous solution of perchloric acid. Products were further purified by column chromatography using silica (mesh size 60–120; Merck).

10-Undecenoic, octadec-*cis*-9-enoic (oleic), and palmitic acids were purchased from Fluka Chemicals (Buchs, Switzerland). Phenylselenyl chloride was purchased from Merck. The FA were esterified by refluxing them with a large excess of anhydrous methanol in the presence of an acid catalyst (19).

*Reaction of methyl 10-undecenoate (**I**) with phenylselenyl chloride in the presence of acetonitrile.* Methyl 10-undecenoate (**I**) (0.498 g, 2.52 mmol) was stirred into a dark red phenylselenyl chloride solution (0.482 g, 2.52 mmol) in acetonitrile (15 mL) until the color changed to pale yellow. *p*-Toluenesulfonic acid (*p*-TSA) (0.479 g, 2.52 mmol) and water (2–4 drops) were then added, and the mixture was stirred at room temperature for 12 h. The solvent was evaporated under reduced pressure. Water (20 mL) was then added to the residue and the reaction mixture was extracted with diethyl ether (3 × 20 mL). The ethereal extract was washed several times with water and dried over anhydrous sodium sulfate. Solvent was evaporated, and the crude extract was subjected to column chromatography using petroleum ether/diethyl ether (9:1, vol/vol) to obtain the pure white crystalline solid product **II** (0.525 g, 50.48%, m.p. 51°C). Calculated for $C_{20}H_{31}O_3NSe$ (**II**): C 58.25%, H 7.52%, N 3.40%; found: C 58.90%, H 7.60%, N 3.20%. IR (neat) (cm^{-1}): 3300 (NH stretching), 1735 ($COOCH_3$), 1578 (aromatic ring) and 1685 and 1575 for C=O amide. NMR ($CDCl_3$): δ 7.6 *m* (2H, hydrogens *ortho* to Se in the phenylselenyl moiety), 7.2 *m* (3H, hydrogens *meta* and *para* to Se in the phenylselenyl moiety), 5.2 *br s* (1H, >N*H*), 3.70 *s* (3H, $COOCH_3$), 3.30–3.26 *m* (1H, >C*H*–N<), 3.05–2.98 *m* (2H, –CH_2–Se–), 2.48 *m* (4H, >N–CH–CH_2– and –CH_2–CO_2CH_3), 1.76 *s* (3H, –NHCOCH_3), 1.28 *br s* (chain –CH_2–). The mass spectrum of compound **II** is presented in Figure 1. The molecular ion peak (M^+) was absent in MS. The structure-justifying fragment ions are shown in Figure 2.

*Reaction of methyl 10-undecenoate (**I**) with phenylselenyl chloride in absolute ethanol.* Methyl 10-undecenoate (**I**) (0.594 g, 3 mmol) was dissolved in dry ethanol (15 mL) in a round-bottomed flask. Phenylselenyl chloride (0.689 g, 3.6 mmol) was added to it, and the reaction mixture was stirred at room temperature for 12 h. At the end of this period the solvent was removed under reduced pressure, and 20 mL of H_2O was added. Further, it was extracted with diethyl ether (3 × 20 mL), and the ethereal extract was washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated to obtain the crude extract, which was then subjected to column chromatography. Elution with a mixture of petroleum ether/diethyl ether (90:10, vol/vol) gave a colorless liquid (**III**) (0.620 g, 50.40%). Calculated for $C_{21}H_{34}O_3Se$: C 61.01%, H 8.28%; found: C 61.08%, H 8.15%. IR (neat) (cm^{-1}): 1740 ($COOCH_3$), 1585,

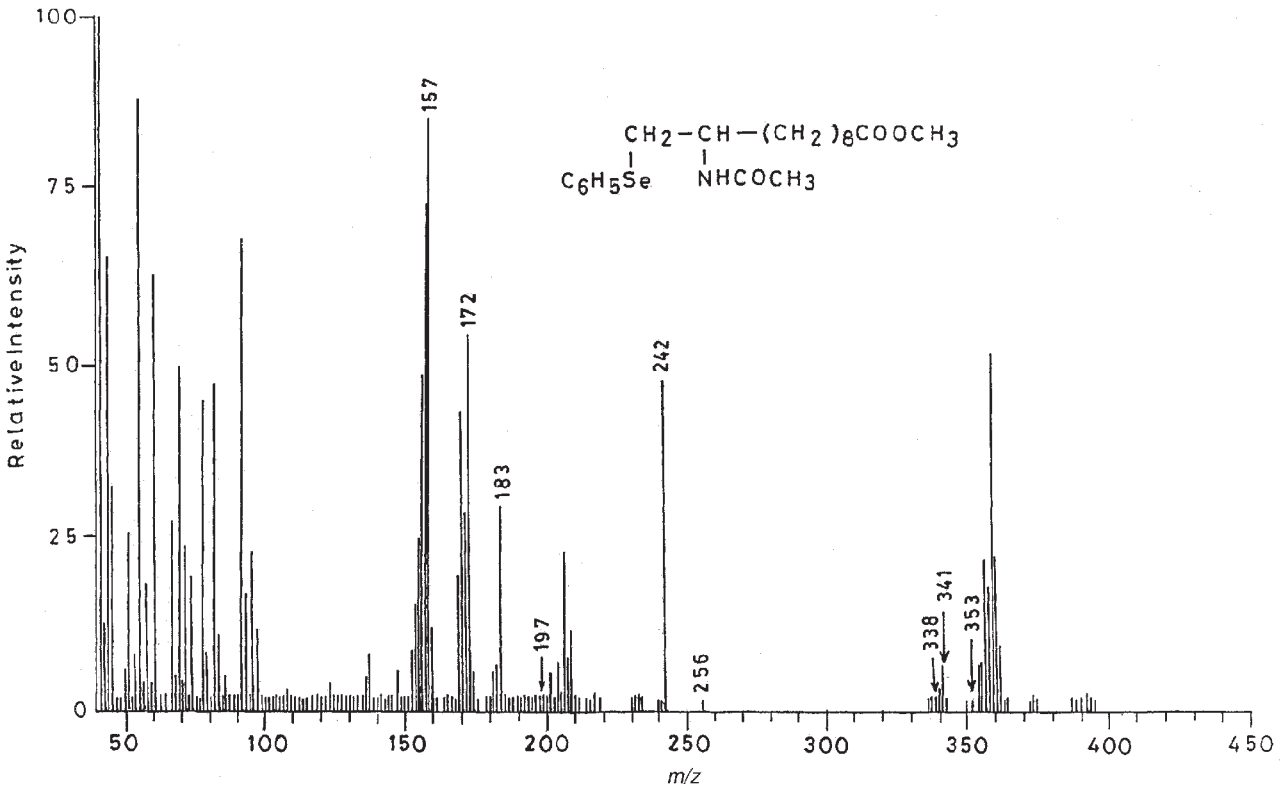


FIG. 1. Mass spectrum of **II** (methyl 11-phenylseleno-10-acetamido-undecanoate).

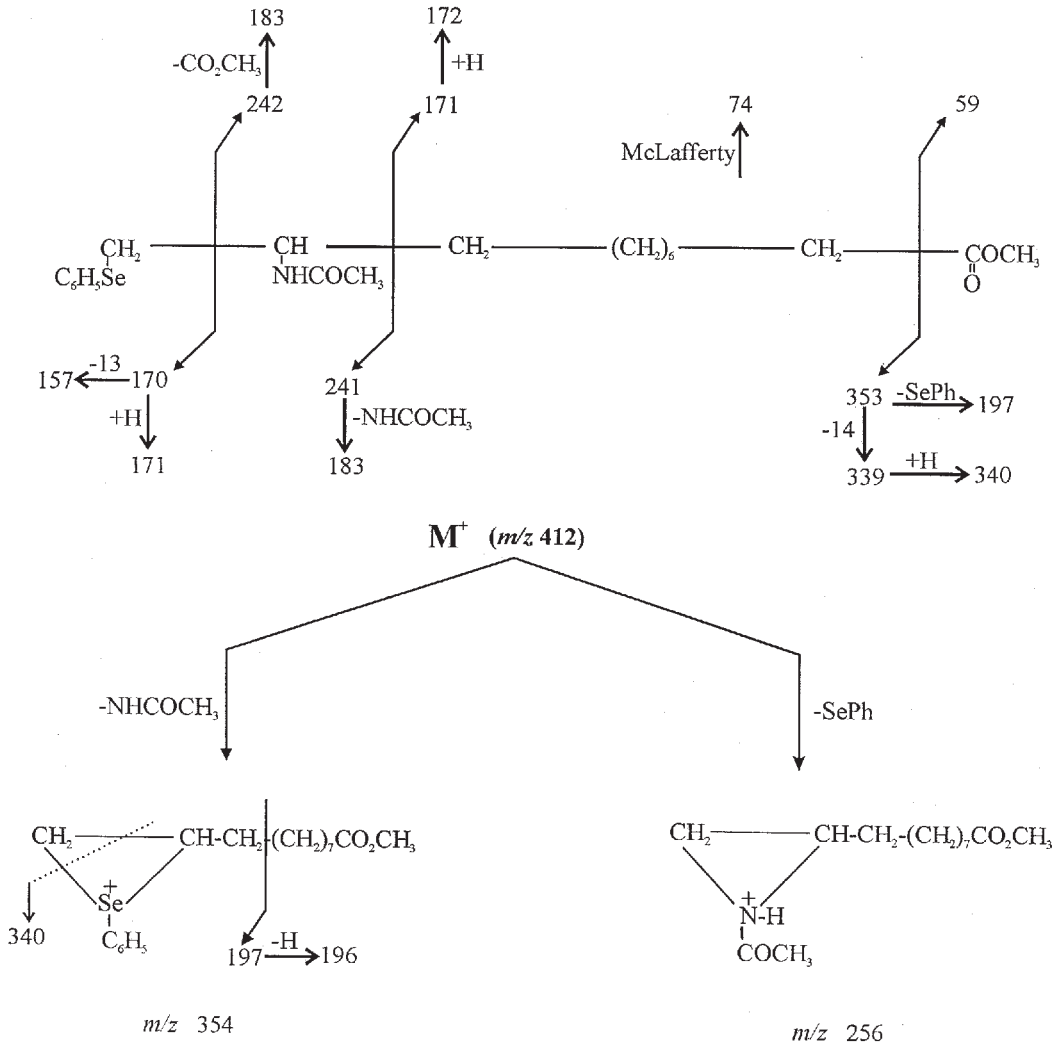


FIG. 2. Mass fragmentation of compound **II**; see Figure 1 for name.

1490, 1005, 735 (aromatic ring). NMR ($CDCl_3$): δ 7.51 *m* (2H, hydrogens *ortho* to Se in the phenylselenyl moiety), 7.35 *m* (3H, hydrogens *meta* and *para* to Se in the phenylselenyl moiety), 4.12 *q* (*J* = 7.2 Hz, 2H, O=C–O$CH_2$$CH_3$), a multiplet centered at 3.48 (3H, >C*H*–OCH_2–), 3.03 *m* (2H, –CH_2–Se–), 2.28 distorted *t* (2H, –CH_2–$CO_2C_2H_5$), 1.58 *m* (4H, –CH_2–CH_2–CO and –OCH–CH_2–), 1.30 *br s* (10H, chain –CH_2–), 1.25 *t* (*J* = 7.2 Hz, 3H, –$CO_2CH_2CH_3$, merged in part with chain CH_2) and 1.16 *t* (*J* = 7.2 Hz, 3H, –OCH_2CH_3). The MS of compound **III** is shown Figure 3, which shows [M + 1] (414) and [M − 1] (412) along with the molecular ion (M^+) peak at *m/z* 413. The important fragment ions are shown in Figure 4.

Reaction of methyl octadec-cis-*9-enoate (**IV**; methyl oleate) with phenylselenyl chloride in absolute ethanol.* A similar reaction of methyl octadec-*cis*-9-enoate (**IV**) (0.894 g, 3 mmol) with phenylselenyl chloride (0.689 g, 3.6 mmol) in absolute ethanol (15 mL) (Scheme 3) was conducted with stirring at room temperature for 18 h. At the end of the reaction, the solvent was removed under reduced pressure and the reaction mixture was processed like methyl 10-undecenoate (**I**). The crude mixture was chromatographed on a column of activated silica gel using petroleum ether/diethyl ether (80:20, vol/vol) to obtain the pure colorless liquid (**V**) (1.73 g, 52.1%). Calculated for $C_{28}H_{48}O_3Se$: C 65.75%, H 9.25%; found: C 65.02%, H 10.1%. IR (neat) (cm^{-1}): 1738 (ester carbonyl), 1474, 1490, 1000, 743 (aromatic). NMR ($CDCl_3$): δ 7.59 *m* (2H, hydrogens *ortho* to Se in the phenylselenyl moiety), 7.36 *m* (3H, hydrogens *meta* and *para* to Se in the phenylselenyl moiety), 4.35 *br m* (2H, >C*H*–C*H*–), 4.12 *q* (2H, –$CO_2CH_2CH_3$), 2.28 distorted *t* (2H, –CH_2–CO), 1.60 *m* (2H, –CH_2CH_2–CO), 1.28 *br s* (24H, chain –CH_2–), 1.17–1.25 (two triplets merged with chain CH_2, 6H, –OCH_2CH_3 and –$CO_2CH_2CH_3$) and 0.88 distorted *t* (3H, terminal CH_3). In the MS of compound **V** both [M + 1] (*m/z* 512) and [M − 1] (*m/z* 510) are present along with a molecular ion (M^+, *m/z* 511) peak. Figure 5 shows the important fragment ions of compound **V**.

Reaction of methyl hexadecanoate (methyl palmitate) with phenylselenyl chloride in absolute ethanol. To support ethyl ester formation in the above reactions, a similar reaction of methyl hexadecanoate (0.813 g, 3 mmol) with phenylselenyl

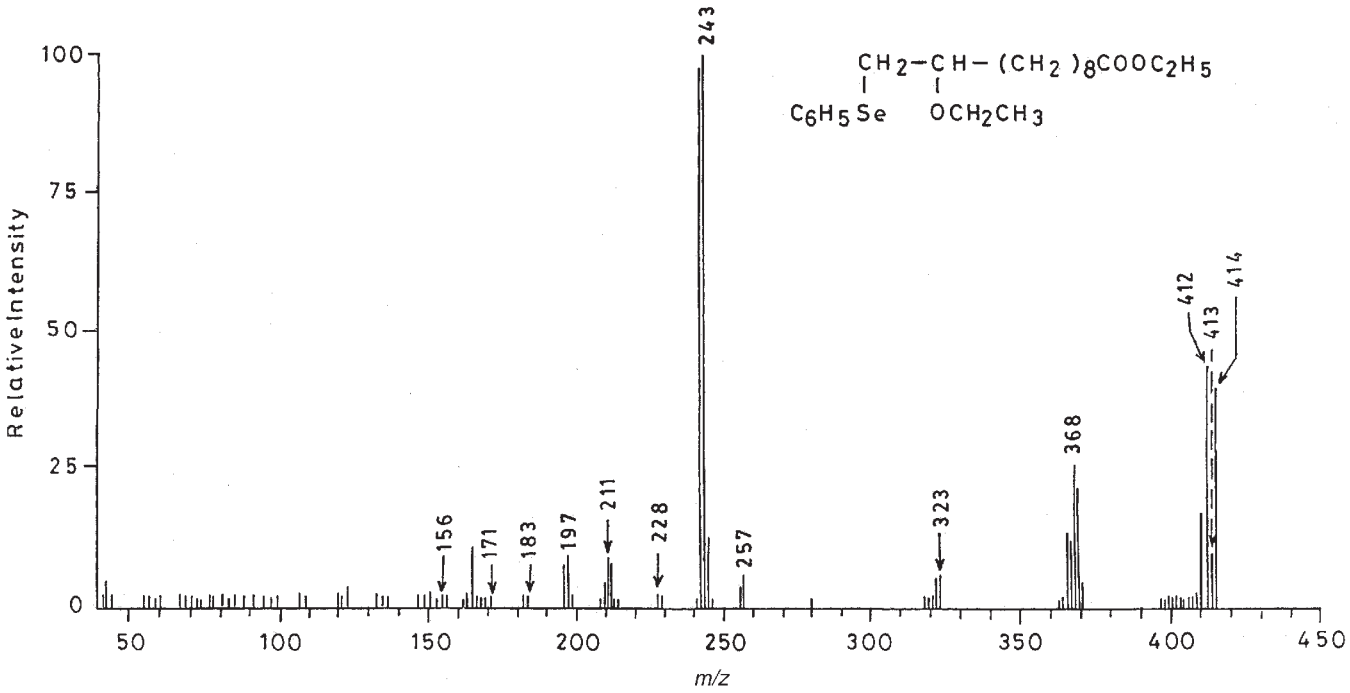


FIG. 3. Mass spectrum of **III** (ethyl 11-phenylseleno-10-ethoxy-undecanoate).

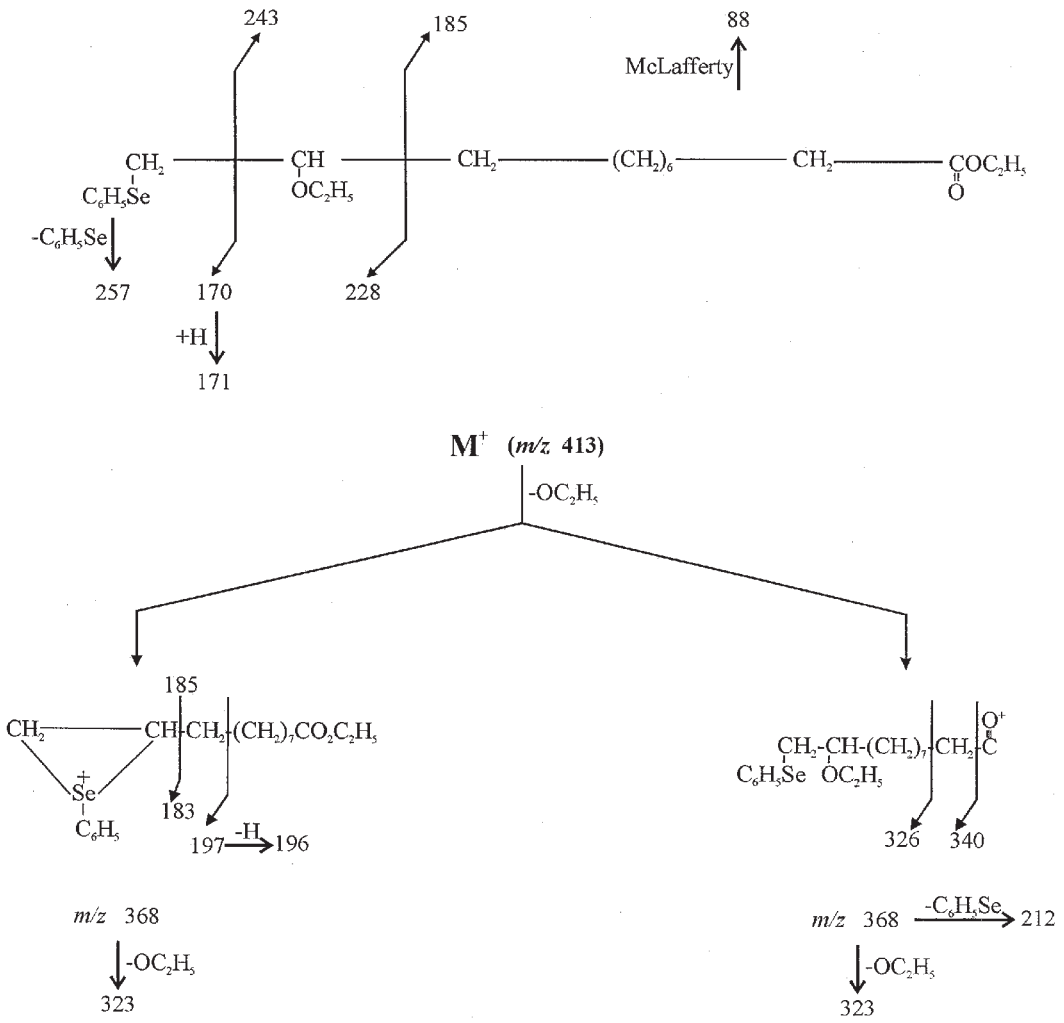


FIG. 4. Mass fragmentation of **III**; see Figure 3 for name.

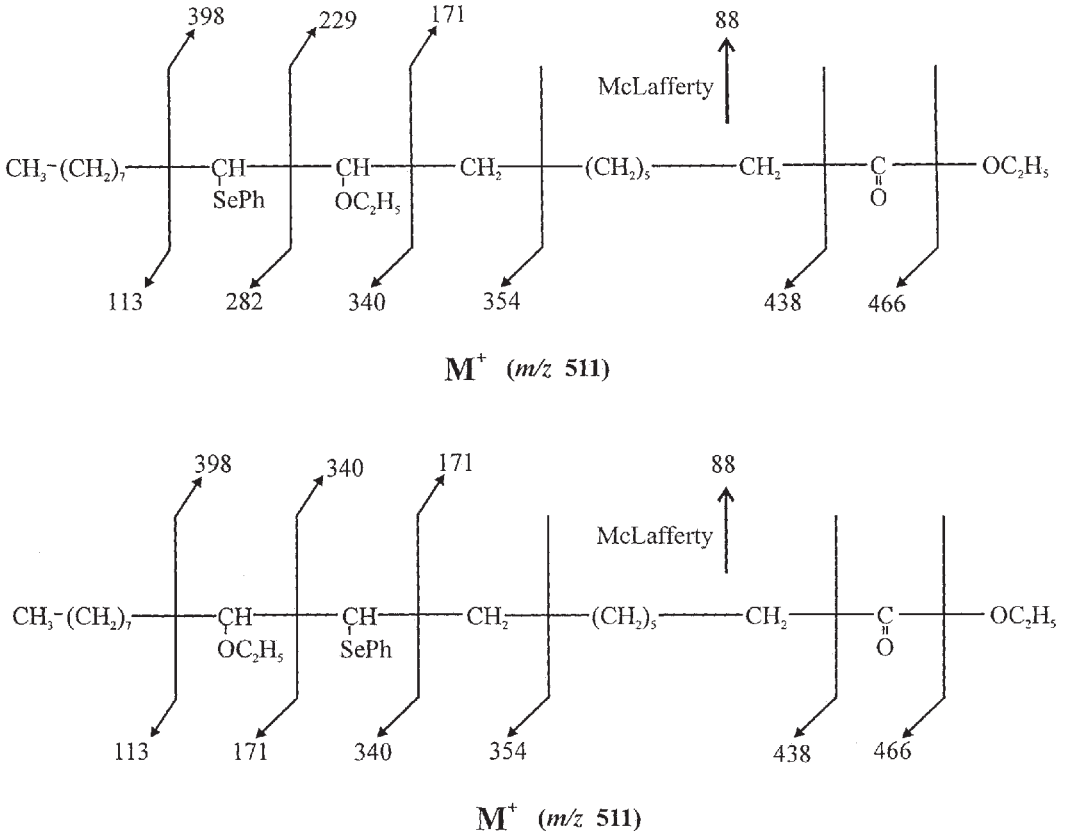


FIG. 5. Mass fragmentation of **V** [ethyl 10(9)-phenylseleno-9(10)-ethoxy octadecanoate].

chloride (0.689 g, 3.6 mmol) in absolute ethanol was conducted to obtain the product **VI** as a colorless liquid in quantitative yield. IR (neat) (cm^{-1}): 1638 (ester carbonyl). NMR ($CDCl_3$): δ 4.11 *q* (*J* = 6.0 Hz, 2H, $-CO_2CH_2CH_3$), 2.28 distorted *t* (2H, $-CH_2-CO$), 1.59 *m* (2H, $-CH_2CH_2CO$), 1.27 *br s* (24H, chain $-CH_2-$), 1.23 *t* (3H, OCH_2CH_3 merged in part with chain CH_2), 0.88 *t* (3H, terminal CH_3).

RESULTS AND DISCUSSION

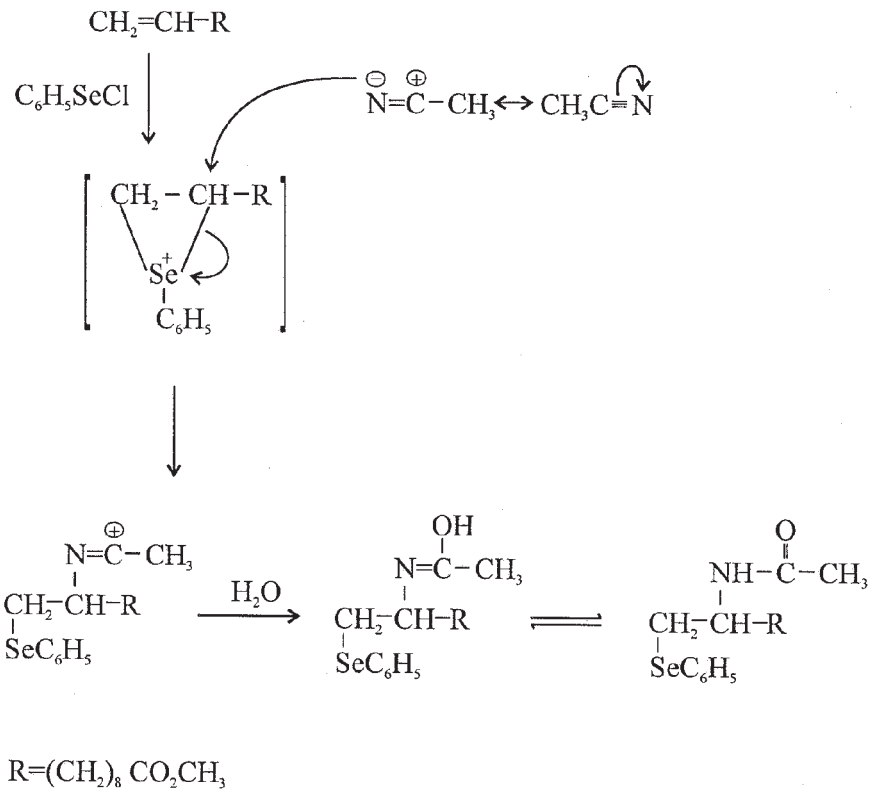
The reaction of **I** with phenylselenyl chloride in acetonitrile gave **II**, whose elemental analysis corresponded to $C_{20}H_{31}O_3NSe$. The evidence in favor of amide formation was initially derived from diagnostic IR bands at 1685 and 1575 cm^{-1}. Monosubstituted benzene was evident from a band at 1578 cm^{-1}. The NMR spectrum of **II** provided further proof by signals at δ 7.6 and 7.2 as multiplets for aromatic protons, 3.30–3.26 *m* (1H, –N–C*H*–), 3.05–2.98 *m* (2H, –Se–CH_2) and 1.76 *s* (3H, –NHCOCH_3). The molecular ion peak (M^+) at *m/z* 412 was absent, but an intense peak due to the loss of $CH_2SeC_6H_5$ from the molecular ion at *m/z* 242 confirmed the presence of a phenylselenyl group at the terminal position. The other salient peaks are shown in Figure 2. On the basis of the above data, the structure of **II** was assigned as methyl 11-phenylseleno-10-acetamido-undecanoate.

Compound **III** was also analyzed for $C_{21}H_{34}O_3Se$, and its IR spectrum illustrated all the characteristic features of an ester group and monosubstituted benzene. The NMR spectrum showed characteristic signals at δ 4.12 *q* (*J* = 7.2 Hz, 2H, O=C–OCH_2CH$_3$), a multiplet centered at 3.48 (3H, >C*H*–OCH_2CH$_3$), 3.03 *m* (2H, –CH_2–Se–), 1.25 *t* (3H, $-CO_2CH_2CH_3$, merged in part with chain CH_2), and 1.16 *t* (3H, *J* = 7.2 Hz, $-OCH_2CH_3$).

MS analysis of **III** (Fig. 4) shows the presence of the molecular ion peak (M^+) at *m/z* 413 along with [M + 1] and [M – 1] peaks. The peaks at *m/z* 243 and 170 confirm the attachment of a phenylseleno group at the terminal carbon. The other diagnostic fragment ions are shown in Figure 4. The spectral data (IR, NMR, MS) confirm that compound **III** is ethyl 11-phenylseleno-10-ethoxy-undecanoate.

The addition of phenylselenyl halides to olefins is a well-studied reaction, which takes place regioselectively (12,20, 21). The addition of phenylselenyl chloride to methyl undecenoate (**I**) proceeds in a similar way. The mechanism suggested for the addition product is shown in Scheme 4. The reaction involves the formation of a cyclic seleniranium ion and the attack of acetonitrile or ethanol on the more substituted carbon. The products were formed according to Markovnikov's rule.

Likewise, treating octadec-*cis*-9-enoate (**IV**) with phenylselenyl chloride in absolute ethanol gave isomeric product **V**, which, on the basis of elemental analysis and spectral data,



SCHEME 4

was characterized as ethyl 10(9)-phenyl-seleno-9(10)-ethoxy octadecanoate. The mass fragmentation of compound **V** (Fig. 5) shows important fragment ions at *m/z* 340, 282, 229, and 171, which confirm the formation of an isomeric product.

Transesterification (i.e., methyl is converted to ethyl ester) took place in the reaction of methyl monoenoate (**I** and **IV**) with phenylselenyl chloride in absolute ethanol. This observation is further confirmed by the reaction of methyl palmitate with phenylselenyl chloride in absolute ethanol; IR and NMR spectral data for this reaction were presented in the Experimental Procedures section. On the basis of these data the structure of the product was assigned as ethyl hexadecanoate (**VI**). Probably in these reactions phenylselenyl chloride is acting as a catalyst.

The prepared compounds can be used as synthetic intermediates and may have some biological activities.

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