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Reaction of 1-Lithio-1-arylthio(or alkylthio)methyltrimethylsilane with Acid Derivatives. A Novel Synthesis of Functionalized Vinyl Sulfides

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Reactions of 1-lithio-1-phenylthiomethyl- (**1a**) and 1-lithio-1-methylthiomethyltrimethylsilane (**1b**) with amides, an ester, acid anhydrides, a urea, and a carbonate are described which provide useful routes to functionalized vinyl sulfides. The reaction of **1** with amides gave β-functionalized vinyl sulfides, 1-dialkylamino-2-phenylthio (or methylthio)ethylenes, in 40—95% yields and the reaction could be extended to the sulfonyl derivatives of **1** to afford 1-dialkylamino-2-phenylsulfonyl(or methylsulfonyl)ethylenes. Although ethyl benzoate and some acid anhydrides were not good substrates for this reaction, tetramethylurea and diethyl carbonate gave α-functionalized vinyl sulfides, 1-amidovinyl- and 1-(ethoxycarbonyl)vinyl sulfides, in moderate yields when treated with **1a** followed by addition of benzaldehyde.

Olefin-forming reaction of α-metallosilanes is known as the Peterson reaction and plays an important role in organic synthesis. For example, 1-lithio-1-arylthio-(or alkylthio)methyltrimethylsilanes **1** react with ketones to give vinyl sulfide derivatives.[1] However, only a few reports mention this type of reactions of the α-metallosilanes **1** with acid derivatives,[2] since they are in general not good substrates for the Peterson olefination.

In our preliminary report we briefly described the reaction of the α-lithiosilanes **1** with several amides which provided a new synthetic method for 2-aminovinyl sulfides.[3] We further investigated the reaction using acid derivatives and found that these reactions can be utilized for preparation of various functionalized vinyl sulfides.

Since vinyl sulfides are very versatile reagents as masked carbonyl compounds,[4] these functionalized vinyl sulfides are expected to have more potential in organic synthesis.[5]

Results and Discussion

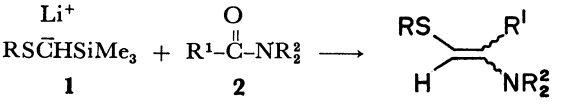
Reaction of the α-Lithiosilane 1 with Amides. 1-Lithio-1-phenylthiomethyltrimethylsilane (**1a**) gener-

TABLE 1. YIELDS, BOILING AND MELTING POINTS, AND SPECTRAL DATA OF **3** AND **8**

R	R^1	R^2_2	Yield %	Isomer ratio[a] E : Z	Bp θ_b/°C (mmHg[b]) [M_p θ_m/°C]	IR(ν/cm^{-1}, neat) C=C	^{1}H NMR (δ, $CDCl_3$)	MS(70 eV) m/e (M^+)
3a PhS	H	Me_2	64	100 : 0	90 (0.01)	1630	2.80(6H,s),4.56(1H,d,J=13.0Hz),6.55 (1H,d,J=13.0Hz),6.8—7.4(5H,m)	179
3b PhS	*t*-Bu	Me_2	40	20 : 80	65—67 (2.0)	1580	1.13(7.2H,s,*Z*-Bu^t),1.19(1.8H,s,*E*-Bu^t), 2.48 (1.2H,s,*E*-Me),2.75 (4.8H,s,*Z*-Me),5.63(0.2H,s,*E*-CH=),5.99(0.8H,s, *Z*-CH=),7.1—7.4(5H,m)	235
3c PhS	Ph	Me_2	65	96 : 4	112—113 (0.03)	1580	2.70 (5.76H,s,*E*-Me),2.85 (0.24H,s, *Z*-Me),5.00 (≈1H,s,*E*-CH=),5.10 (≈0H, *Z*-CH=),6.8—7.4(10H,m)	255
3d PhS	Ph	$-(CH_2)_2-$	87	80 : 20	145 (0.1)	1580	1.90 (3.2H,s,*E*-CH_2),2.11 (0.8H, s,*Z*-CH_2),5.73(0.8H,s,*E*-CH=),5.91 (0.2H, s,*Z*-CH=),7.0—7.7(10H,m)	253
3e PhS	Ph	$-(CH_2)_5-$	95	100 : 0	130 (0.02)	1580	1.2—1.8(6H,m),2.6—3.2(4H,m),5.21 (1H,s,CH=),6.8—7.5(10H,m)	295
3f MeS	Ph	$-(CH_2)_5-$	72[a]	87 : 13	120 (2.0)	1580	1.2—1.8 (6H,m),2.10 (2.6H,s,*E*-Me), 2.27 (0.4H,s,*Z*-Me),2.6—3.2(4H,m), 5.03(≈0.9H,s,*E*-CH=),5.12(≈0.1H,s, *Z*-CH=),7.2—7.5(5H,m)	233
8a $PhSO_2$	H	Me_2	60	100 : 0	[131]	1610[c]	2.86(6H,s),4.84(1H,d,J=12.0Hz,CH=), 7.1—8.0(6H,m,CH= and Ph)	211
8b $PhSO_2$	H	$-(CH_2)_5-$	81	100 : 0	150 (1.0)[d]	1600	1.2—1.8 (6H,m),2.9—3.3(4H,m),4.95 (1H,d,J=13.0 Hz,CH=),7.1—8.0(6H, m,CH= and Ph)	251
8c $MeSO_2$	H	Me_2	42	100 : 0	173 (1.0)[e]	1600	2.90(9H,s),4.90(1H,d,J=12.0Hz,CH=), 7.17(1H,d,J=12.0 Hz,CH=)	149
8d $MeSO_2$	H	$-(CH_2)_5-$	24	100 : 0	150 (1.0)[d]	1610	1.4—1.8(6H,m),2.92 (3H,s),3.0—3.3 (4H,m),4.98 (1H,d,J=12.8 Hz,CH=), 7.11(1H,d,J=12.8 Hz,CH=)	189

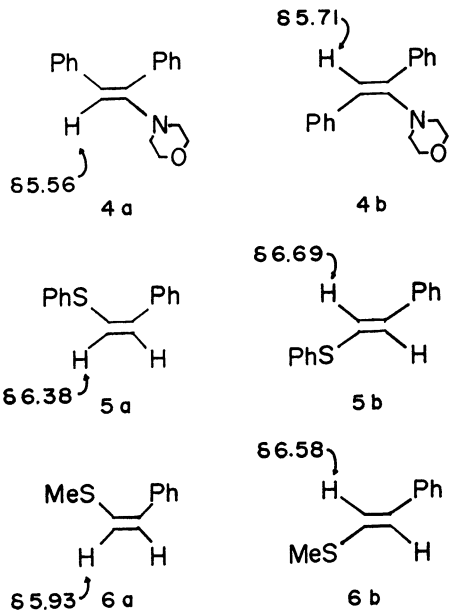
a) Determined by NMR spectroscopy. b) 1 mmHg≈133.322 Pa. c) In Nujol mull. d) Purified by pot distillation. e) Purified by Kugel Rohr.

ated by treating phenylthiomethyltrimethylsilane with butyllithium at 0 °C in THF was reacted with *N,N*-dimethylformamide at the same temperature and was allowed to stand overnight. Usual work-up of the reaction mixture gave 64% of (*E*)-1-dimethylamino-2-phenylthioethylene (**3a**). In this reaction only the (*E*)-isomer was obtained and the structure was determined by spectral data and elemental analysis. Similarly several 2-aminovinyl sulfides were obtained from the α-lithiosilanes **1** and amides **2** in good yields under very mild conditions and the results are summarized in Table 1.



1a: R=Ph
1b: R=Me

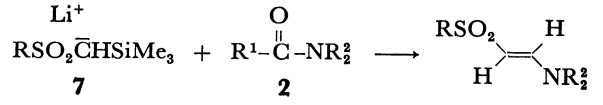
In most cases a mixture of (*E*)- and (*Z*)-isomers was obtained and the ratio was determined by NMR spectroscopy. Estimation of the coupling constant between the phenyl carbon and the vinyl proton ($^3J_{CH}$) by ^{13}C-NMR measurement under selective irradiation of the phenyl protons was tried. However, the values for the compounds **3c** (the major isomer only) and **3e** were ≃7 cps which was not decisive for determination of (*E*)- or (*Z*)-form of olefinic compounds. The assignment of (*E*)- and (*Z*)-isomers of the compounds **3c**—**f** was done by comparison of the chemical shifts of the vinyl protons with those of the known compounds **4**,[6] **5**,[7] and **6**.[8] Thus the isomer which



shows the vinyl proton signal in the higher field is determined to be the (*E*)-isomer of **3** (the vinyl proton is *trans* to the phenyl ring) and the other is the (*Z*)-isomer. For the vinyl sulfide **3b**, the methyl group which appears in the lower field is suggested to be that of the (*Z*)-isomer by comparing chemical shifts of the alkylamino groups of **3c** and **3d**. Hence the major product of the reaction was found to be an (*E*)-isomer except for the case of **3b**.

Although the sterically less favorable (*E*)-isomers were predominant, this result is consistent with the observation that **4a**, sterically less favorable, is thermodynamically more stable than **4b**, which is sterically less crowded.[6] This phenomenon was explained by the continuous overlap between the electron pair on the nitrogen atom and the phenyl group in its polar resonance form[9] and the same reason can be applied to the predominance of the (*E*)-isomers in this reaction. The only exception observed for **3b** may be ascribed to the large steric repulsion caused by the bulky *t*-butyl group which suppressed the formation of the (*E*)-isomer.

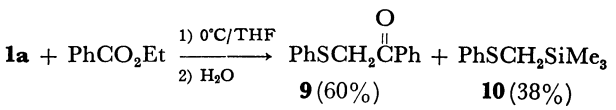
Extension of the reaction to sulfone derivatives was successful. The reaction of 1-lithio-1-phenylsulfonyl(or methylsulfonyl)methyltrimethylsilane **7** with amides **2** gave 2-aminovinyl sulfones **8** and the results are listed



7a: R=Ph
7b: R=Me

in Table 1. Method of lithiation and reaction conditions are different from the preceding reactions (see Experimental). Contrary to the α-phenylthiosilane **1a**, the corresponding phenylsulfonylsilane **7a** gave very poor yields of vinyl sulfones when treated with less reactive amides such as *N,N*-dimethylbenzamide and *N*-benzoylpiperidine. Oxidation of the aminovinyl sulfides to sulfones were also examined, but it was difficult to isolate or to purify the oxidized products. Thus the present reaction is one of the better routes to 2-aminovinyl sulfones.

Reaction with Ester and Acid Anhydride. Reaction of the α-lithiosilane **1a** with ethyl benzoate was carried out in a similar manner to the reaction with amides, and α-phenylthioacetophenone (**9**) was obtained in 60% yield with considerable amount of the starting phenylthiomethylsilane **10**. The anticipated product, 2-ethoxyvinyl sulfide, was not formed at all or the sulfide is quite sensitive to hydrolysis even under basic conditions, since no vinyl proton signals were detected in the NMR spectrum of the reaction mixture immediately after the quenching. Addition of benzaldehyde or

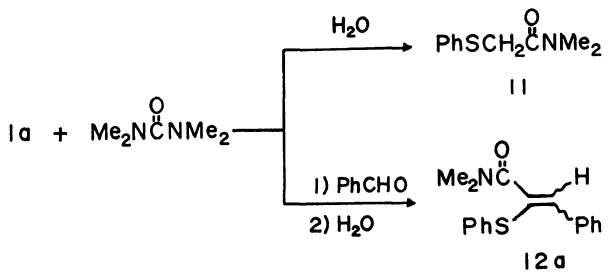


successive addition of lithium diisopropylamide and the aldehyde to the reaction mixture before the quenching was also carried out, but no vinyl sulfide derivatives were detected. Hence, it is not possible that the initial product of the reaction was an acylated phenylthiomethyltrimethylsilane which corresponds to **16** or **18** in Scheme shown later.

Similar reaction of the silane **1a** with benzoic anhydride gave only a small amount of α-phenylthioacetophenone (**9**) and the most part of **1a** was recovered as the starting phenylthiomethylsilane **10**. Some cyclic acid anhydrides such as phthalic anhydride and maleic anhydride were found to be quite unreactive with **1a**.

$$\mathbf{1a} + (PhCO)_2O \xrightarrow[2)H_2O]{1)\ rt/THF} \mathbf{9}(18\%) + \mathbf{10}(77\%)$$

Reaction with Urea and Carbonate. The α-lithiosilane **1a** was treated with tetramethylurea at room temperature to give *N,N*-dimethyl-α-phenylthioacetamide (**11**) in 56% yield. As it was likely that the reaction proceeded *via* substitution of the dimethylamino group, benzaldehyde was added to the reaction mixture and was allowed to stand for one day at room temperature. The product was *N,N*-dimethyl-α-phenylthiocinnamamide (**12a**, 41%) and thus one pot synthesis of an 1-amidovinyl sulfide was found. The same treatment of the methylthiomethylsilane **1b** and the urea gave *N,N*-dimethyl-α-methylthiocinnamamide (**12b**, 27%).



Similarly, the silane **1a** reacted with diethyl carbonate to afford ethyl α-phenylthiocinnamate (**13**) after addition of benzaldehyde. The yield was increased by addition of an equimolar amount of lithium diisopropylamide (LDA) because of its higher basicity than that of lithium ethoxide generated by substitution.

$$\mathbf{1a} + EtO\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt \longrightarrow$$

$$[PhSCH(SiMe_3)CO_2Et + EtOLi] \xrightarrow{LDA}$$

$$[PhSCLi(SiMe_3)CO_2Et] \xrightarrow[2)\ H_2O]{1)\ PhCHO} EtO\overset{O}{\overset{\|}{C}}(PhS)C{=}CHPh$$

13 (59%)

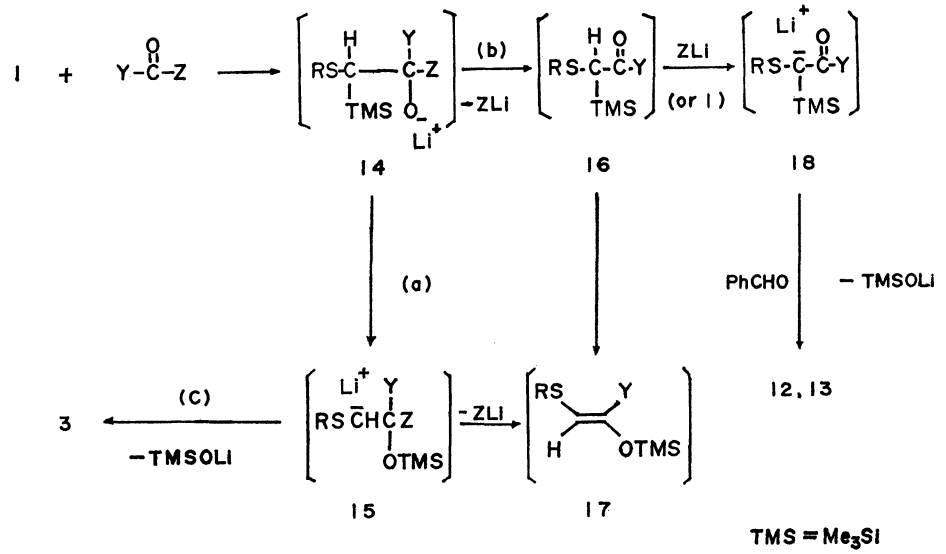
The paths for the whole reactions are assumed to be as shown in Scheme 1. The two paths from the initially formed intermediate **14** is considered to be controlled by the nature of the substituents Y and Z. When Y is not a hetero-atom substituent, rearrangement of the intermediate **14** to **15** occurs to form an olefinic compound **3** or **17**. Thus the reaction with an amide proceeded *via* the paths (a) and (c). On the other hand, the path (b) seems to be predominant when both Y and Z are hetero atoms such as the urea and the carbonate. Formation of 1-acylvinyl sulfides on addition of benzaldehyde implies the intermediacy of **18** and excludes the formation of **11** by hydrolysis of a 1,1-diaminoethylene corresponding to **3**. The path for the reaction with the ester, however, is not clear at the moment. The result that no olefinic product was obtained by addition of lithium diisopropylamide and benzaldehyde suggests less possibility of the formation of **16** or **18**. But we cannot exclude the formation of α-phenylthioacetophenone (**9**) by hydrolysis of a vinyl ether **3** or a silyl ether **17**.

Experimental

Boiling points were uncorrected. A melting point was determined on a Yanagimoto micro melting point apparatus and was uncorrected. ^1H and ^{13}C NMR spectra were obtained with JEOL JNM PMX-60 and JNM FX-90Q FT spectrometers using TMS as an internal standard. IR spectra were taken on a JASCO IRA-1 spectrophotometer. Mass spectrometry was performed on a Hitachi RMU-6E spectrometer at an ionizing voltage of 70 eV.

All experiments were carried out under a dry nitrogen atmosphere.

Materials. Commercially available butyllithium, ethyl benzoate, tetramethylurea, diethyl carbonate, and *N,N*-dimethylformamide were used. The other amides were prepared by the reaction of the corresponding acid chlorides and the amides and purified by distillation except for *N*-benzoylaziridine. Isopropylamine and THF were dried and distilled by the usual method. Phenylthiomethyltrimethylsilane, methylthiomethyltrimethylsilane, phenylsuflonylmethyltrimethylsilane, and methylsulfonylmethyltrimethylsilane



Scheme 1.

were prepared by silylation of methyl phenyl sulfide, dimethyl sulfide, methyl phenyl sulfone, and dimethyl sulfone with triemethylsilyl chloride, respectively, by the known method.[10]

General Procedure for the Reactions of the Silanes **1** *with Acid Derivatives.* To a stirred solution of phenylthio(or methylthio)methyltrimethylsilane (**1**, 5.0 mmol) in THF (5 ml) was added butyllithium (3.8 ml of 15% hexane solution, 6.0 mmol) at 0—5 °C, and the solution was stirred for 2 h at room temperature. An acid derivative (5.0 mmol) in THF (5 ml) was added at 0—5 °C and the stirring was continued for 2 h at the same temperature. The mixture was stood overnight at room temperature, quenched with water after cooling, and extracted (ether). The oragnic layer was dried (Na_2SO_4) and evaporated to give a crude product, which was isolated and purified by distillation and/or chromatography on silica gel. 1-Dialkylamino-2-phenylthio(or methylthio)-ethylenes **3** could be purified only by distillation because of their ready hydrolysis. Hence, some of their elemental analyses were unsatisfactory.

*1-Dimethylamino-2-phenylthioethylene (**3a**)*: Found: C, 66.88; H, 7.43; N, 7.53; S, 18.15%. Calcd for $C_{10}H_{13}NS$: C, 67.02; H, 7.31; N, 7.82; S, 17.86%.

*α-Dimethylamino-β-phenylthiostyrene (**3c**)*: ^{13}C NMR ($CDCl_3$) δ 40.7 (q), 86.8 (d, =CHS–), 158.2 (s, =CPh), and aromatic carbons at δ 123.9, 125.2, 127.6, 127.9, 128.2, 128.8, 136.6 and 141.2. Found: C, 75.17; H, 6.72; N, 5.54; S, 12.38%. Calcd for $C_{16}H_{17}NS$: C, 75.27; H, 6.71; N, 5.49; S, 12.53%.

*β-Phenylthio-α-piperidinostyrene (**3e**)*: ^{13}C NMR ($CDCl_3$) δ 24.5 (t), 25.8 (t), 50.2 (t), 91.2 (d, =CHS–), 158.2 (s, =CPh), and aromatic carbons at δ 124.4, 126.0, 127.8, 128.3, 128.5, 129.3, 137.1, and 140.7. Found: C, 76.81; H, 7.04; N, 4.54; S, 10.90%. Calcd for $C_{19}H_{21}NS$: C, 77.26; H, 7.12; N, 4.74; S, 10.83%.

*α-Phenylthioacetophenone (**9**)*: Bp 120 °C/1.0 mmHg by pot distillation; IR (neat) 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.30 (2H, s, CH_2), 7.1—7.5 (8H, m, PhS and a part of PhCO), 7.8—8.0 (2H, m, the rest of PhCO); MS, *m/e* 228 (M^+).

N,N-*Dimethyl-α-phenylthioacetamide (**11**)*: Bp 120 °C/3 mmHg, IR (neat) 1630 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.92 (3H, s), 2.98 (3H, s), 3.71 (2H, s), 7.0—7.6 (5H, m).

The Reactions of the Silanes **7** *with Amides.* To a stirred butyllithium (3.8 ml of 15% hexane solution) was added diisopropylamine (0.84 ml, 6.0 mmol) in THF (5 ml) at 0—5 °C. After stirring for 1 h at room temperature, the resulting lithium diisopropylamide (LDA) solution was cooled to −60—−70 °C and phenylsulfonyl(or methylsulfonyl)trimethylsilane (5.0 mmol) was added to the solution. The stirring was continued for 1 h at room temperature followed by addition of an amide (6.0 mmol) in THF (5 ml). Then the mixture was warmed at 50—60 °C for 5 h with stirring. The reaction mixture was quenched with water after cooling, extracted (CH_2Cl_2), dried (Na_2SO_4), and concentrated to give a crude product, which was isolated and purified by crystallization or distillation. Elemental analyses of the products were not satisfactory because of their high sensitivity to hydrolysis.

*1-Dimethylamino-2-phenylsulfonylethylene (**8a**)*: Found: C, 56.69; H, 6.18; N, 6.63; S, 15.10%. Calcd for $C_{10}H_{13}NO_2S$: C, 56.86; H, 6.20; N, 6.63; S, 15.15%.

Formation of the Cinnamamides **12** *and the Cinnamate* **13**. Benzaldehyde (5.0 mmol) in THF (5 ml) was added to a reaction mixture obtained from phenylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), and tetramethylurea (5.0 mmol) according to the procedure shown above. The mixture was allowed to stand for 1 d at room temperature and was worked up similarly to the previous runs to give 0.58 g (41%) of *N,N*-dimethyl-α-phenylthiocinnamamide (**12a**) as a mixture (57 : 43) of two isomers: bp 130 °C/0.001 mmHg by pot distillation; IR (neat) 1630 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.63 (≈1.7H, s), 2.76 (≈1.7H, s), 2.89 (≈1.3H, s), 2.95 (≈1.3H, s), 6.60 (0.57H, s), 6.73 (0.43H, s), 7.1—7.7 (10H, m).

An analytical sample of the major isomer could be isolated by chromatography on silica gel; MS, *m/e* 283 (M^+). Found: C, 71.84; H, 5.01; N, 6.11; S, 11.01%. Calcd for $C_{17}H_{17}NOS$: C, 72.06; H, 4.94; N, 6.05; S, 11.29%.

Similarly 0.30 g (27%) of *N,N*-dimethyl-α-methylthiocinnamamide (**12b**) was obtained from methylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), the urea (5.0 mmol), and the aldehyde (5.0 mmol) as a mixture (65 : 35) of two isomers: bp 150 °C/5 mmHg; IR (neat) 1620 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.24 (1.05H, s), 2.35 (1.95H, s), 2.81 (1.95H, s), 2.98 (≈2H, s), 3.04 (≈1H, s), 3.13 (≈1H, s), 6.48 (0.65H, s), 6.59 (0.35H, s), 7.1—7.6 (5H, m), MS, *m/e* 221 (M^+).

In the case of the reaction starting with phenylthiomethyltrimethylsilane (5.0 mmol), butyllithium (6.0 mmol), and diethyl carbonate (5.0 mmol), THF solution of LDA (5.0 mmol) prepared by the method shown above was added to the reaction mixture at 0 °C. The mixture was stirred for 3 h at the same temperature and overnight at room temperature followed by addition of benzaldehyde (5.0 mmol) in THF (5 ml). The mixture was allowed to stand for 1 d at room temperature and worked up as the previous runs to afford 0.84 g (59%) of ethyl α-phenylthiocinnamate (**13**): bp 150 °C/1 mmHg by pot distillation; IR (neat) 1720 cm^{-1} (C=O); ^1H NMR δ 1.30 (3H, t), 4.07 (2H, q), 7.3—7.9 (10H, m), 8.30 (1H, s, =CH); MS, *m/e* 284 (M^+).

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