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Irina Novosjolova<sup>a</sup> & Māris Turks<sup>a</sup>

<sup>a</sup> Faculty of Material Science and Applied Chemistry, Riga Technical University, Paula Valdena Str. 3, Riga, LV-1007, Latvia

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## USER FRIENDLY SYNTHESIS OF VOGEL'S SILYL SULFINATE AND ITS APPLICATION IN QUANTITATIVE GC-MS ANALYSIS

Irina Novosjolova, Māris Turks\*

Faculty of Material Science and Applied Chemistry, Riga Technical University, Paula Valdena Str. 3, Riga, LV-1007, Latvia; e-mail: maris turks@ktf.rtu.lv

### Abstract

The synthesis of trimethylsilyl 2-methylprop-2-ene-1-sulfinate (Vogel's silyl sulfinate) from methallyltrimethylsilane and SO<sub>2</sub> in the presence of  $Tf_2NTMS$  was developed. The title compound silylates carbohydrates and other polyhydroxylated compounds by producing SO<sub>2</sub> and isobutene as gaseous side products. This silylation procedure is perfectly suitable for derivatization and subsequent GC-MS quantitative analysis of ribose and malic acid as representatives of organic polyhydroxylated compounds.



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### Keywords

Trimethylsilyl 2-methylprop-2-ene-1-sulfinate, silylation, GC-MS derivatization, ribose, malic

acid

### INTRODUCTION

The use of gas chromatography (GC) with capillary columns in the quantitative and qualitative analysis of carbohydrates and other polyhydroxylated organic substances is often superior to other analytical techniques due to its sensitivity especially if it is coupled with mass spectrometric (MS) detection.<sup>1</sup> On the other hand, organic molecules possessing several polar functional groups such as -OH, -COOH, -NH<sub>2</sub>, and -SH are characterized by low volatility. They also tend to interact with GC column material thus producing asymmetric chromatographic signals with extensive tailing.<sup>2</sup> The extensively used derivatization procedure to enhance the volatility of organic substances for their gas chromatographic analysis is silvlation.<sup>2,3</sup> Trimethylsilyl derivatives of polyhydroxylated compounds are characterized by excellent thermal stability and ionization when MS detection is used. Various silvlation procedures and derivatization technologies have been developed up to now, including the injection port derivatization.<sup>2</sup> Regardless the fact that the first silvlation was introduced in 1944, the search for improved silvlation conditions and novel reagents is still ongoing.<sup>4</sup> Very often one commercially available silyl group donor should be combined with others and only the resulting silylating cocktail is efficient as derivatization reagent for quantitative GC-analysis.<sup>5</sup> In 2005. Vogel and coworkers reported efficient and traceless silvlation of simple alcohols, phenols and carboxylic acids with trimethylsilyl 2-methylprop-2-ene-1-sulfinate (Vogeløs silyl sulfinate).<sup>6</sup> The aim of the present research is to develop an user-friendly gram-scale synthesis of the title reagent and to demonstrate its applications in quantitative GC-MS analysis of polyhydroxylated organic compounds.

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### **RESULTS AND DISCUSSION**

The previously reported syntheses of Vogeløs silyl sulfinate **2** were using either sufficiently strong Lewis acids to execute the sila-*ene* reaction between allylsilanes and SO<sub>2</sub> at low temperatures in liquid SO<sub>2</sub> or weak Lewis acids that required to carry out this reaction in a pressure reactor.<sup>7</sup> By careful choice of Lewis acid and solvent we have found that the synthesis of **2** can be accomplished at ambient temperature by a simple bubbling of gaseous SO<sub>2</sub> through a toluene solution of **1** in the presence trimethylsilyl bis(trifluoromethanesulfonyl)imide (Tf<sub>2</sub>NSiMe<sub>3</sub>; Gosez Lewis acid) (Scheme 1).<sup>8</sup> Methallylsilane (**1**) was mixed with bis(trifluoromethanesulfonyl)imide (Tf<sub>2</sub>NH) to produce the required catalyst *in situ* before the sila-*ene* reaction. After applying the flow of SO<sub>2</sub> for 2 h the reaction mixture was directly fractionally distilled under reduced pressure to provide product **2** in 71% yield. The developed synthetic procedure is suitable for preparation of **2** in at least 30-40 g scale.

With the compound **2** in hand we proceeded to its applications as GC-MS derivatization reagent. The presence of high number of functional groups and several tautomeric forms in solution makes carbohydrates as excellent examples for the GC-derivatization method evaluation.<sup>9</sup> Additionally, per-O-silylated monoscaharides have found useful applications in synthetic organic chemistry.<sup>10</sup> When a suspension of D-ribose in CH<sub>3</sub>CN (or CD<sub>3</sub>CN) was treated with an excess of Vogeløs silylsulfinate **2** clean GC-MS traces and <sup>1</sup>H-NMR spectrum were obtained after 2 h at ambient temperature. The only co-products were isobutene and SO<sub>2</sub>. Both analyses independently showed a mixture of isomers in a ratio 35:65. Their structures were attributed as per-O-silylated -D-ribopyranose ( $\alpha$ -**3**) and per-O-silylated -D-ribopyranose ( $\beta$ -**3**), respectively (Scheme 2).

This prompted us to evaluate the potential application of **2** as the derivatization reagent for quantitative GC-MS analysis. Indeed, GC-MS analysis of D-ribose samples that were treated with **2** in CH<sub>3</sub>CN provided good linear correlation (Figure 1a). The error of quantification of D-ribose was below 0.5%. Further we have chosen L-malic acid as an example of hydroxy dicarboxylic acid for quantification experiment after derivatization with **2** (Scheme 3). Also in this case, the series of derivatized samples provided excellent linear correlation and the experimental error of quantification of L-malic acid was below 1.5% (Figure 1b).

In conclusion we have developed an user-friendly synthetic procedure towards Vogeløs silyl sulfinate **2**. We have demonstrated for the first time its application as the derivatization reagent in the quantitative GC-MS analysis of polyhydroxylated organic compounds with D-ribose and L-malic acid as the representative examples.

### EXPERIMENTAL

### Trimethylsilyl 2-methylprop-2-ene-1-sulfinate (2).

A three neck round-bottom flask was charged with a gas inlet tube and *Vigreux* column the top of which contains the Liebigøs condenser. The system was evacuated *in vacuo*, flame-dried, and cooled under N<sub>2</sub> atmosphere. A solution of bis(trifluoromethanesulfonyl)imide (Tf<sub>2</sub>NH) (4.0 g, 14.2 mmol, 6 mol-%) in anh. toluene (30 mL) was slowly added to a solution of methallyltrimethylsilane (44 mL, 0.25 mol, 1.06 equiv. (~2.5 mL, 14.2 mmol is consumed by Tf<sub>2</sub>NH)) in anh. toluene (50 mL) at ambient temperature. An exotermic reaction with evolution of isobutene was observed and the resulting reaction mixture was stirred at ambient temperature for 20 min to ensure the formation of Tf<sub>2</sub>NSiMe<sub>3</sub>. Then gaseous SO<sub>2</sub> was bubbled through the

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resulting mixture at ambient temperature over 1,5-2 h. Initially (the first 30-45 min.) a slightly exothermic reaction was observed. The gas inlet tube was removed, the system was attached to vacuum and toluene was distilled at 35 °C (55-60 mbar; bath temp. 80 °C). Then the pressure was adjusted to 1.2 Torr and Vogeløs silyl sulfinate **2** was collected in the following fractions: I fraction (2.6 g, b.p. 35-41 °C, GC purity 93.0%), II fraction (17.0 g, b.p. 41-49 °C, GC purity 98.6%), III fraction (13.1 g, b.p. 49-50 °C, GC purity 99.6%). The total yield calculated on pure substance: 32.2 g (71%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): 5.06 (m, 1H, Ha-C(3)), 4.96 (m, 1H, Hb-C(3)), 3.38, 3.33 (2dd, AB syst., *J*=12.0, 1.0 Hz, 2H, H-C(1)), 1.84 (dd, *J*=1.5, 1.0 Hz, 3H, H<sub>3</sub>C-C(2)), 0.30 (s, 9H, H<sub>3</sub>C-Si). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100.6 MHz): 134.4, 117.9, 69.3, 23.5, 0.6.

### Silylation of D-ribose.

Reagent 2 (52 L, 304 mol, 8 equiv.) was added to a suspension of D-ribose (5.77 mg, 38 mol) in CD<sub>3</sub>CN (1 mL). The resulting mixture was kept for 2 h at ambient temperature and then analyzed by GC-MS and NMR. GC-MS conditions: capillary column HP-5MS (5% phenylmethylsiloxane) 30 m × 0,25 mm × 0,25 m; injector temp. 250 °C; eluent He, flow rate 0.8 ml/min; split injection 400:1; injection volume 0.2 L; temp. regime: 70 °C 0 min, gradient 20 °C/min 250 °C, gradient 120 °C/min 310 °C, 310 °C for 1 min; MS-detector (ESI, 70 eV); MS Quad 150 °C; MS Source 230 °C. For the construction of the calibration curve the corresponding solutions (CH<sub>3</sub>CN) were prepared in volumetric flasks (10 mL) and kept at 50 °C for 2 h prior analysis. The GC-MS correlation area for each data point was obtained in triplicate.

### Silylation of L-malic acid and construction of the calibration curve.

Reagent 2 (5 equiv) was added to a suspension of precisely weighted sample of malic acid in  $CH_3CN$  and the volumetric flask (10 mL) was filled to the mark with  $CH_3CN$ . The resulting

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derivatization mixture was kept for 30 min at ambient temperature and analyzed by GC-MS (see above): split injection 600:1; injection volume 1.0 L; temp. regime: 50 °C 3 min, gradient 50 °C/min 250 °C, 250 °C for 1 min, gradient 50 °C/min 310 °C, 310 °C for 1 min.

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### REFERENCES

- Zou, P.; Yang, X.; Huang, W.-W.; Zhao, H.-T.; Wang, J.; Xu, R.-B.; Hu, X.-L.; Shen, S.-Y.; Qin, D. *Molecules* 2013, 18, 9933-9948.
- 2. Wang, Q.; Ma, L.; Yin, C.-r.; Xu, L. J. Chromatogr. A 2013, 1296, 25-35.
- a) Poole, C. F. J. Chromatogr. A 2013, 1296, 2-14; b) Halket, J. M.; Zaikin, V. G. Eur. J. Mass Spectrom. 2003, 9, 1-21.
- 4. Van Look, G. Simchen, G. Heberle, J. Silylating Agents, Fluka, Buchs: Switzerland, 2nd ed., 1995.
- a) Toledano, R. M.; Cortés, J. M.; Andini, J. C.; Vázquez, A.; Villén, J. J. Chromatogr. A 2012, 1256, 191-196; b) Tzing, S.-H.; Ding, W.-H. J. Chromatogr. A 2010, 1217, 6267-6273; c) Wu, J.; Hu, R.; Yue, J.; Yang, Z.; Zhang, L. J. Chromatogr. A 2009, 1216, 1053-1058.
- 6. Huang, X.; Craita, C.; Awad, L.; Vogel, P. Chem. Commun. 2005, 1297-1299.
- a) Bouchez, L.C.; Reddy Dubbaka, S.; Turks, M.; Vogel, P. J. Org. Chem. 2004, 69, 6413-6418; b) Markovi , D.; Volla, C. M. R.; Vogel, P.; Varela-Álvarez, A.; Sordo, J. A. Chem. Eur. J. 2010, 16, 5969; c) Bouchez, L.; Vogel, P. Synthesis 2002, 225-231.
- 8. Mathieu, B.; Ghosez, L. Tetrahedron 2002, 58, 821968226.
- a) Ruiz-Matute, A. I.; Hernández-Hernández, O.; Rodríguez-Sánchez, S.; Sanz, M. L.; Martínez-Castro, I. J. Chromatogr. B 2011, 879, 122661240; b) Medeiros, P. M.; Bernd R.T. Simoneit, B. R. T. J. Chromatogr. A 2007, 1141, 2716278.
- 10. Kulkarni, S. S.; Gervay-Hague, J. Org. Lett. 2008, 10, 4739-4742.

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Figure 1. a) GC-MS traces of per-*O*-silylated ribopyranose, b) Calibration curves for quantitative analysis of D-ribose and L-malic acid.

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Scheme 1. Synthesis of Vogel's silyl sulfinate

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Scheme 2. Derivatization of D-ribose with TMS-groups and the NMR analysis (600 MHz, CD<sub>3</sub>CN) of the products:  $\delta^{1}$ H: x.xx;  $\delta^{13}$ C: *y.yy*;  $\delta^{29}$ Si: <u>z.zz</u>.

# <sup>11</sup> ACCEPTED MANUSCRIPT



Scheme 3. Derivatization of L-malic acid with 2

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