Pergamon

Tetrahedron Letters 41 (2000) 8307–8309

TETRAHEDRON LETTERS

First synthesis of an *O*-glycosylated glucosinolate isolated from *Moringa oleifera*

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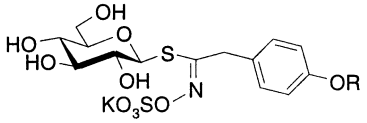
Received 11 July 2000; accepted 1 September 2000

Abstract

Starting from L-rhamnose, the first synthesis of the major glucosinolate (**1**) isolated from *Moringa oleifera* seeds was effected in seven steps.

Glucosinolates constitute a homogeneous class of naturally occurring thiosaccharidic compounds mainly found in the botanical order Brassicales: they can be hydrolyzed by myrosinase (thioglucoside glucohydrolase E.C. 3.2.3.1.) to produce D-glucose and various degradation products—particularly isothiocyanates—depending on the aglycon part.[1]

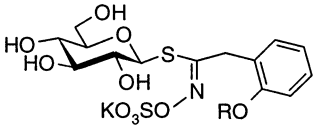
Moringa oleifera (Moringaceae) is a multipurpose tree widespread throughout most of the tropics,[2] the seeds of which contain 8–10% of a structurally unusual glucosinolate **1**—an *O*-rhamnosylated form[3] of glucosinalbin **2**.



(**1**) R = α-L-rhamnopyranosyl

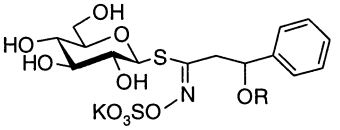
(**2**) R = H

Compound **1** is a representative member in a group of glucosinolates whose aglycon bears an *O*-glycosylated hydroxyl function. Other examples arise from the family Resedaceae: glucosinolate **3**—an *O*-rhamnosylated form of isoglucosinalbin **4**—was identified in the genus *Reseda*,[4] whereas **5**—an *O*-arabinosylated derivative of glucobarbarin **6**—was shown to be present in the genus *Sesamoides*.[5]



(**3**) R = α-L-rhamnopyranosyl

(**4**) R = H



(**5**) R = α-L-arabinopyranosyl

(**6**) R = H

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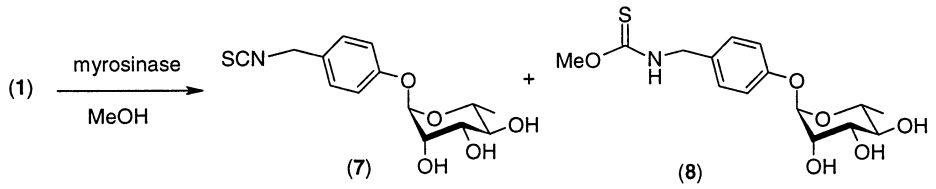
0040-4039/00/$ - see front matter
PII: S0040-4039(00)01466-0

Unlike glucosinolates **3** and **5**—which were isolated and spectroscopically characterized, compound **1** has previously only been postulated as the likely precursor to bioactive molecules such as isothiocyanate **7** and thionocarbamate **8** (Scheme 1).[6]



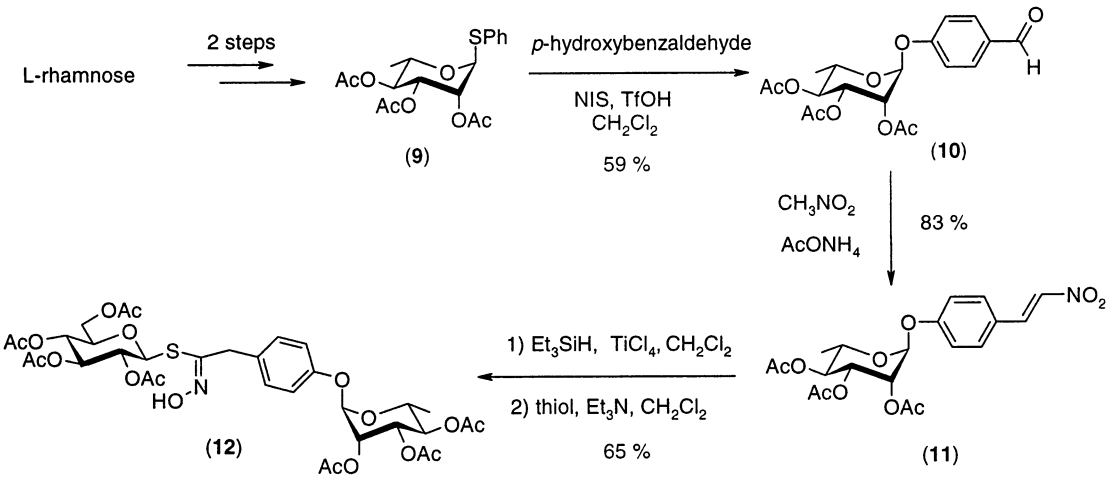
Scheme 1.

Extraction and purification of glucosinolate **1** from *M. oleifera* seeds was performed according to a well established protocol;[7] after purity assessment by reversed phase HPLC according to the ISO 9167-1 method, compound **1** was fully characterized by ^{1}H and ^{13}C NMR and mass spectrometry.[8]

In former years, our group has been strongly involved in synthesizing both natural and artificial glucosinolates.[9] The elaboration of a synthetic sequence to produce *O*-glycosylated glucosinolates is challenging in several aspects: we thus decided to undertake the synthesis of **1** with a view to producing final evidence of structure.

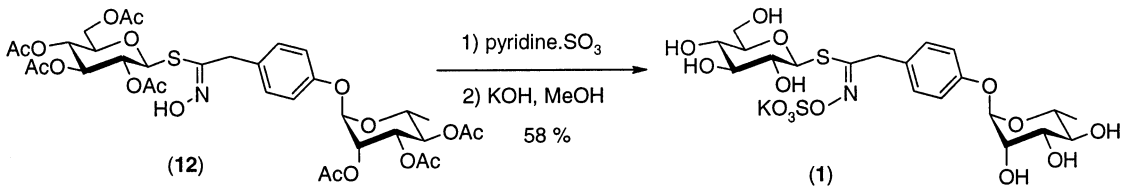
The synthetic pathways to glucosinolates which have been developed within recent decades are constantly based on a key coupling step between 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose ('thiol') and a highly reactive hydroximoyl chloride, furnishing stereospecifically a (*Z*)-thiohydroximate precursor.[10]

Starting from L-rhamnose, the previously described[11] aryl α-L-rhamnoside **10** was obtained in reasonable yield through a convenient modification of Kunz' approach[6]—i.e. *N*-iodosuccinimide activation of the corresponding phenyl thioglycoside **9**.[12] The *p*-*O*-rhamnosylated *E*-nitrostyrene **11** was produced from compound **10** under the mildly basic conditions prescribed by Lappin,[13] then **11** was converted into the corresponding hydroximoyl chloride[14] to be condensed right away with the protected thiol following the methodology recently developed in our laboratory.[15] The precursor **12** was obtained from **10** in 54% overall yield (Scheme 2).



Scheme 2.

The hydroximino group of **12** was *O*-sulfated using a SO_3–pyridine complex, to yield after aqueous $KHCO_3$ neutralization the peracetylated form of the glucosinolate. Standard transesterification conditions finally afforded the target molecule **1**, whose spectral data (MS, NMR) were found to be identical to those measured on a natural sample (Scheme 3).



Scheme 3.

By using the synthetic sequence described above, the structure of the major glucosinolate extracted from *M. oleifera* seeds has been unequivocally ascribed. Our methodology appears versatile enough to consider a possible extension to the building up of many analogues of **1** either diversely *O*-glycosylated or modified on the thio-sugar moiety.[16] This is being currently investigated in our group.

Acknowledgements

A grant (D.G.) from the French MENRT is acknowledged. We also thank Dr. J. C. Jacquinet for helpful discussions, Dr. A. Quinsac (CETIOM) and S. Cassel for analytical assistance.

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3. The presence of a 4′-*O*-acetylated derivative of **1** was also postulated in *Moringa peregrina*; see Kjaer, A.; Malver, O.; El Menshawi, B.; Reisch, J. *Phytochemistry* **1979**, *18*, 1485–1487.
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8. $[\alpha]=-47$ (*c* 1.0, H_2O); MS (Ionspray® mode): 570 ($M-H^+$); ^1H NMR (250 MHz): δ: 1.26 (d, 3H, H-6′), 3.26 (m, 1H, H-5), 3.32–3.48 (m, 3H, H-2, H-3 and H-4), 3.55 (t, 1H, $J=9.7$, H-4′), 3.64–3.72 (m, 2H, H-6), 3.83 (m, 1H, H-5′), 4.03 (dd, 1H, $J=3.5$, H-3′), 4.13 (s, 2H, H-8), 4.20 (dd, 1H, $J=1.9$, H-2′), 4.74 (m, 1H, H-1), 5.58 (bs, 1H, H-1′), 7.18 (d, 2H, $J=8.5$, H-11), 7.40 (d, 2H, H-10); ^{13}C NMR (62.89 MHz): 18.2 (C-6′), 39.0 (C-8), 61.8 (C-6), 70.2 (C-4), 70.9 (C-5′), 71.5 (C-2′), 71.6 (C-3′), 73.3 (C-2), 73.5 (C-4′), 78.5 (C-3), 82.9 (C-1), 83.4 (C-5), 99.6 (C-1′), 119.1 (C-11), 130.9 (C-9 and C-10), 156.2 (C-12), 164.2 (C-7).
9. For a recent example, see Aucagne, V.; Gueyrard, D.; Tatibouët, A.; Quinsac, A.; Rollin, P. *Tetrahedron* **2000**, *56*, 2647–2654.
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