Synthesis of 2-Hydroxy-3-butenylglucosinolates

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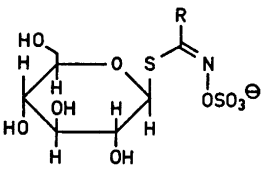
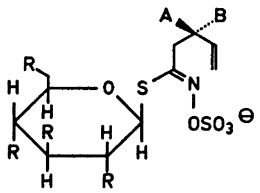
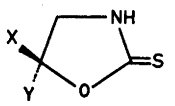
Since the first synthesis of a glucosinolate, *viz.* (I, R: $C_6H_5CH_2$), was reported in 1957 by Ettlinger and Lundeen,[1] several additional glucosinolates have become synthetically available, mostly such containing simple aryl, aralkyl, and alkyl side-chains. However, the synthesis of allylglucosinolate, (I, R: $CH_2=CHCH_2$), by Benn and Ettlinger,[2] constituted structurally and partly methodically, an interesting extension, subsequently adopted by us for the synthesis of 3-butenylglucosinolate (I, R: $CH_2=CH(CH_2)_2$).[3] Within the large, but structurally uniform class of naturally occurring glucosinolates, those containing 2-hydroxy-3-butenyl side-chains (I, R: $CH_2=CHCHOHCH_2$) are of considerable practical significance.[4] We now report the synthesis of an unresolved, approximately equimolar mixture of (*R*)- and (*S*)-2-hydroxy-3-butenylglucosinolate.



(I)



(II)

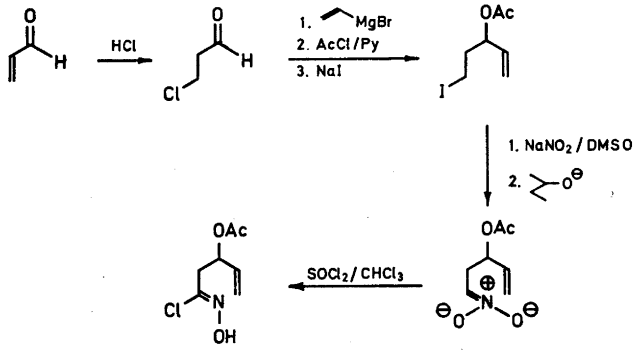


$(III)_R$: X = H ; Y = $CH=CH_2$

$(III)_S$: X = $CH=CH_2$; Y = X

As in previous cases,[2,3] the β-thioglucosidic linkage was established by reacting tetra-*O*-acetyl-1-thio-β-D-glucopyranose with the requisite, unsaturated hydroxamoyl chloride. The latter, in form of the acetate (IV), was produced through the sequence of reactions shown below.

The resulting amorphous mixture of epimeric pentaacetates on sulphonation afforded a crystalline mixture of the corresponding sodium glucosinolate pentaacetates, (II_R: R = A = $CH_3CO{\cdot}O$, B = H) and (II_S: R = B = $CH_3CO{\cdot}O$, A = H), $[\alpha]_D^{22}$ −12.5° (H_2O). Potassium salts of the supposedly pure stereoisomerides, produced by acetylation of the individual, naturally occurring 2-hydroxy-3-butenylglucosinolates, are reported with specific rotation values (in water) of −14.8° (or −15.1°, for another preparation),[5] and −9.5°,[6] for (II_S) and (II_R), respectively. Deacetylation of the synthetic pentaacetate mixture yielded an amorphous sodium glucosinolate fraction which was, in turn, subjected to enzymic



(IV)

hydrolysis with a crude myrosinase preparation. In keeping with the structure (II), previously shown to yield (*S*)- (III_S), and (*R*)-5-vinyloxazolidine-2-thione, (III_R), on enzymic hydrolysis of the (*R*)- and (*S*)-epimer, respectively,[5] a partly racemic mixture, $[\alpha]_D^{20}$ $-5°$ ($CHCl_3$) of (III_R) and (III_S) was obtained, consisting of a 47:53 mixture of the two enantiomers, based on the reported, specific rotation values of $+75.1°$ and $-76.8°$ for the supposedly homogeneous stereoisomers, (III_R) and (III_S), respectively.[5] The synthetic glucosinolate fraction exhibited no signs of separation upon chromatography.

*Experimental.** *3-Acetoxy-5-chloro-1-pentene.* An ethereal solution of vacuum-distilled 2-chloropropanal [7] (92.5 g in 100 ml) was added, in the course of 2 h, to a stirred solution of vinylmagnesium bromide, kept at 10–20°. The latter was prepared from vinyl bromide (103 g) and magnesium (24.3 g) in THF (300 ml),[8] and was diluted with ether (200 ml) before use. After additional stirring for 0.5 h, the reaction mixture was poured into excess aqueous NH_4Cl. The organic phase was extracted into ether (250 ml); the extract was washed with aq. $NaHCO_3$ and water, dried, and concentrated in vacuum. Distillation afforded the desired 5-chloro-3-hydroxy-1-pentene (37 g), b.p. 67–69°/11 mm, which, without further characterization, was converted into its acetate by adding acetyl chloride (65 ml) to its cooled solution in anhydrous pyridine (75 ml). After normal work-up, and distillation *in vacuo*, 3-acetoxy-5-chloro-1-pentene (39 g) was obtained as a colourless liquid, b.p. 81–82°/12 mm, n_D^{26} 1.4415. (Found: C 51.80; H 6.88; Cl 22.07. Calc. for $C_7H_{11}ClO_2$: C 51.71; H 6.82; Cl 21.80). The NMR-spectrum contained the expected signals at: δ 2.08 (*s*, 3H, CH_3CO-), 2.12 (*m*, 2H, $-CH_2CH_2Cl$), 3.37 (*t*, 2H, $-CH_2Cl$), and 5.1–6.2 ppm (*m*, 4H, $-CH(OAc)-$, and $H_2C=CH-$).

3-Acetoxy-5-iodo-1-pentene. The above chloride (69.6 g), dissolved in acetone (500 ml), containing sodium iodide (200 g), was refluxed overnight. After work-up, the iodide was purified by distillation (98 g), b.p. 70–72°/1.2 mm, n_D^{23} 1.5048. (Found: C 33.07; H 4.40; I 50.05. Calc. for $C_7H_{11}IO_2$: C 33.09; H 4.36; I 49.95). NMR-spectrum: δ 2.08 (*s*, 3H, CH_3COO-), 2.20 (*m*, 2H, $-CH_2CH_2I$), 3.17 (*t*, 2H, $-CH_2I$), and 5.1–6.1 ppm (*m*, 4H, $-CH(OAc)-$, and $H_2C=CH-$).

3-Acetoxy-5-nitro-1-pentene. Following the directions of Kornblum *et al.*,[9] the above iodide (50.8 g) was added, in the course of 15 min, to a stirred and cooled solution of $NaNO_2$ (24 g) in dimethyl sulphoxide (200 ml). Stirring was continued at room temperature for 2.5 h, when the reaction mixture was poured into ice-water (500 ml) and extracted three times with a total of 300 ml of a 3:2 mixture of petroleum ether and chloroform. After extraction with water (2 × 150 ml) and drying, solvents were removed *in vacuo*, and the residue was subjected to fractional distillation. The fraction (11.3 g) with b.p. 85–86°/0.6 mm consisted of the nitro-compound with a purity of 95–98 % according to gas chromatography. A homogeneous specimen was prepared by chromatography on silica gel, with benzene:ether (9:1) as the eluting phase, n_D^{23} 1.4493. (Found: C 48.58; H 6.41; N 7.93. Calc. for $C_7H_{11}NO_4$: C 48.55; H 6.40; N 8.09). NMR-Spectrum: δ 2.07 (*s*, 3H, CH_3COO-), 2.40 (*m*, 2H, $-CH_2CH_2NO_2$), 4.45 (*t*, 2H, $-CH_2NO_2$), and 5.1–6.2 ppm (*m*, 4H, $-CH(OAc)-$, and $H_2C=CH-$).

S-(*Tetra-O-acetyl-β-D-glucopyranosyl*)-*3-acetoxy-4-pentenothiohydroximic acids.* A solution of the above nitro-compound (5.2 g) in ether (50 ml) was added, with stirring, to a solution of Na (0.7 g) in 2-butanol (25 ml).* Addition of anhydrous ether (500 ml) caused the sodium salt to separate. It was filtered off under nitrogen, washed with ether, and dried over P_2O_5 (4.3 g).

The powdered salt (2.2 g) was added to a solution of thionyl chloride (3 ml) in chloroform (60 ml), kept below $-30°$. After 5 min, unreacted salt was removed by filtration, and the filtrate was poured into ice-water (100 ml). The dried chloroform solution of the hydroxamoyl chloride (IV) was in turn added to a stirred solution of tetra-*O*-acetyl-1-thio-β-D-gluco-pyranose (2.5 g) in chloroform (50 ml), cooled to $-10°$ before triethylamine (6 ml) was added. Stirring was continued for an additional 0.5 h; the reaction mixture was washed with ice-cold 1 N H_2SO_4 (2 × 250 ml) and water, and dried. After removal of the solvent, an aliquot (1 g) of the sirupy residue (3.8 g) was chromatographed on silica gel, with benzene:ether (3:1) as the mobile phase. Thus, the thiohydroximic acid fraction (340 mg) was obtained as an amorphous solid, sintering at 75–90°. (Found: C 48.40; H 5.80; N 2.72; S 6.18. Calc. for $C_{21}H_{29}NO_{12}S$: C 48.55; H 5.63; N 2.70; S 6.17), $[\alpha]_D^{25}$ $-6.3°$ (*c* 1.6, $CHCl_3$). The complex NMR-spectrum exhibited the expected signals.

* Melting points are uncorrected. NMR-Spectra are recorded in $CDCl_3$-solutions at 60 MHz.

* 2-Butanol was used, rather than methanol or ethanol, in order to minimize undesired alcoholysis of the acetate groups.

Sodium 2-hydroxy-3-butenylglucosinolate O-*pentaacetates* (II, R=A=CH_3CO·O; B=H) and (II, R=B=CH_3CO·O; A=H). Non-purified thiohydroximic acid, containing about 1.3 g, was stirred overnight in pyridine (40 ml) with SO_3:pyridine complex (3.0 g). The mixture was neutralized with 10 % $NaHCO_3$ (50 ml) and extracted with ether. The aqueous phase was concentrated to dryness at <40°. The sirupy residue was combined with additional material, obtained by resulphonation of the material obtained from the ether extracts, and passed, in aqueous solution, through acid alumina (200 g) (Woelm). The column was rinsed with water (350 ml) and the glucosinolate acetates were eluted with 1 % NaOH. The whole procedure was repeated, yielding, after evaporation to dryness, a lightly yellow syrup (812 mg) which was taken up in ethanol. Addition of ether and prolonged cooling resulted in the separation of a crystalline glucosinolate pentaacetate fraction (340 mg) which was recrystallized twice from 2-propanol before analysis (m.p. 162–170° (rapid heating)), $[\alpha]_D^{22}$ −12.5° (*c* 2.0, H_2O). (Found: C 40.23; H 4.68; N 2.16; S 10.10. Calc. for $C_{21}H_{28}NO_{15}S_2Na$: C 40.57; H 4.54; N 2.25; S 10.32). On paper chromatography in butanol : ethanol : water (4 : 1 : 4), and spraying with ammoniacal $AgNO_3$, only one spot was observed.

Deacetylation and enzymic hydrolysis. The above pentaacetate mixture (56 mg) was dissolved in MeOH (3 ml), saturated at 0° with ammonia. Paper chromatography served to establish when ammonolysis of the ester groupings had gone to completion. The residue from the reaction mixture was dissolved in a citrate buffer (pH 6.4), a few drops of a cell-free myrosinase solution and a trace of ascorbic acid were added, and the mixture set aside at room temperature for 3 h. The solution was extracted twice with $CHCl_3$. Evaporation, after drying, gave a residue (4.5 mg) from which traces of elementary S were removed by extraction with CS_2. The crystalline residue (3.8 mg) gave one spot on TLC-chromatography, indistinguishable from that of (+)- or (−)-5-vinyl-2-oxazolidinethione, (III_R) and (III_S), and possessed the rotation value $[\alpha]_D^{20}$ −5° (*c* 0.3, $CHCl_3$). The mass spectrum was identical with that of the authentic compounds (III_R) and (III_S).

Microanalyses were performed by Mr. G. Cornali and his staff.

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On the Crystal Structures of $Rb_2Cr_3O_{10}$ and $Rb_2Cr_4O_{13}$

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The crystal structures of rubidium trichromate(VI), $Rb_2Cr_3O_{10}$, and rubidium tetrachromate(VI), $Rb_2Cr_4O_{13}$, have been investigated. Three-dimensional intensity data were collected with a Siemens automatic diffractometer with Nb-filtered Mo$K\alpha$ radiation. The structures were determined from three-dimensional Patterson syntheses, and the atomic positions were refined by use of full-matrix least-squares program. The results are summarized in Tables 1 and 2. For the sake of brevity isotropic temperature factors are given although anisotropic factors were finally used as indicated by the figures.

The trichromate ion consists of three CrO_4 tetrahedra sharing corners (Fig. 1). The Cr – O (terminal) distances range from