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Aliphatic Hydroximates: Structure and Interconversion of Stereoisomers

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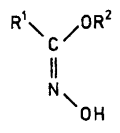
Aliphatic alkyl hydroximates, produced by reaction of alkyl imidates with hydroxylamine, or by alkylation of alkyl hydroxamates, exist as *Z*- and *E*-isomers. Structural assignment rests on analogies in physical properties, as compared with those of the methyl *E*- and *Z*-acetohydroximates; the structure of the latter is unambiguously established by X-ray crystallography.

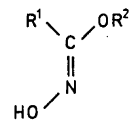
Consistently, the more stable isomers possess the *E*-configuration. In most cases they are partly convertible into the *Z*-isomers upon protonation. Intramolecular, bifunctional catalysis supposedly accounts for the lability of the *Z*-isomers of β-D-glucopyranosyl phenylacetohydroximates. The reversal of the relative stability, when compared with thiohydroximates, is commented upon.

The crystals of methyl *Z*-acetohydroximate are hexagonal, space group $P6_3/m$ with $a = 10.913(3)$, $c = 6.837(3)$ Å, $Z = 6$. The structure was solved by direct phasing technique using three-dimensional X-ray diffraction data and was refined by full-matrix least-squares methods. The final *R*-value is 0.063. The crystal structure is composed of layers of molecules, which form cyclic, hydrogen-bonded trimers. The conformation of the $CH_3-O-C=N-O-H$ moiety is *ap Z ap*.

An unambiguous structure determination of the ethyl hydroximates (*1Z* and *1E*), brought about by X-ray crystallography,[1,2] provided a secure foundation for assignment of structure to several pairs of analogous isomers of alkyl benzohydroximates, including a number of *O*-alkyl and *O*-acyl derivatives, on the basis of dipole moment measurements,[3] the propensity to undergo Beckmann rearrangement,[4,5]



Z



E

1, $R^1 = Ph$; $R^2 = Et$
2, $R^1 = Me$; $R^2 = Et$
3, $R^1 = R^2 = Me$
4, $R^1 = PhCH_2$; $R^2 = Me$
5, $R^1 = PhCH_2$; R^2 = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl

melting point consistencies,[3,5] stereomutation processes,[3,5] acidity properties,[3] and, to a limited extent, ^1H NMR spectroscopy.[5,12]

For the limited group of known aliphatic alkyl hydroximates, of particular interest to us in connexion with other studies, the extant data are less consistent. Thus, the ethyl acetohydroximate, prepared by Houben and Schmidt,[6] was subsequently shown [7] to produce an *O*-phosphate on treatment with PCl_5, rather than a carbamate, favouring its formulation as the *E*-isomer (*2E*). Repetition of the synthesis by Millen and Waters,[8] however, gave an 8:1 mixture of isomers, the more abundant of which was assigned the *Z*-configuration (*2Z*), on the basis of a questionable ^1H NMR analogy to the oxime series; on storage, stereomutation of the alleged *2E* to *2Z* was observed.[8] Conversely, a patent claim, comprising *O*-carbamoyl derivatives of aliphatic alkyl hydroximates,[9] contains a tentative assignment of *E*-configuration to the predominant Houben-synthesis hydroximates, partly convertible, upon protona-

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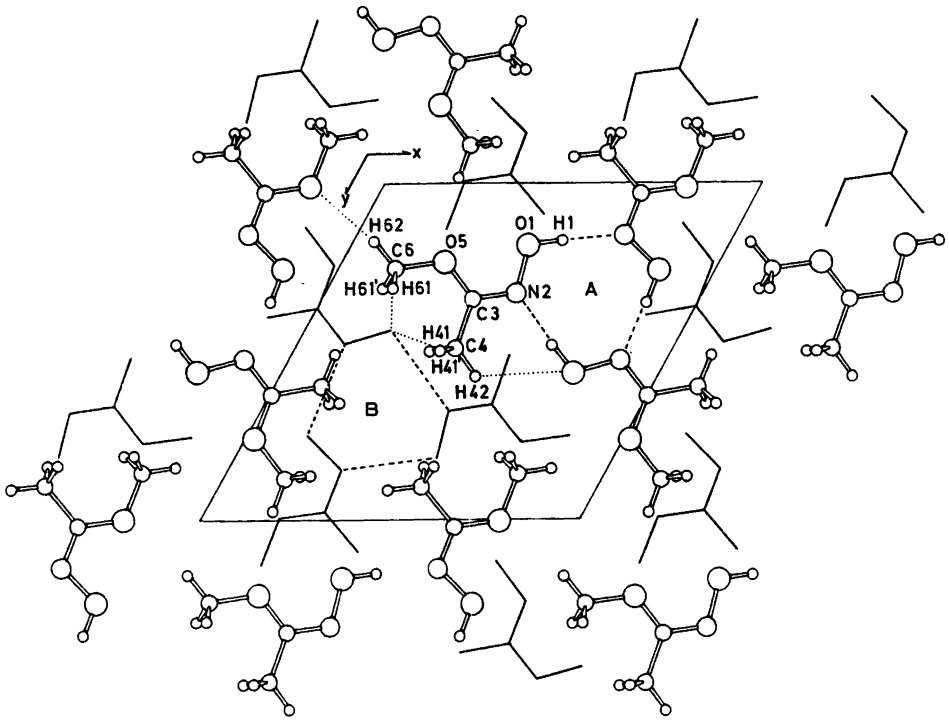


Fig. 1. The structure of methyl *Z*-acetohydroximate as viewed along an axis deviating 10° from the direction of the c axis to allow all the hydrogen atoms of the methyl groups to be seen. Dashed lines indicate hydrogen bonds, dotted lines indicate contacts between methyl hydrogen atoms and neighbouring oxygen atoms. Symbols A and B represent trimers from two layers, separated by 3.418 Å.

tion, into the *Z*-isomers. We report our endeavours to clear up these inconsistencies.

RESULTS

Conversion of methyl and ethyl acetimidate into the corresponding hydroximates, in yields of 25 and 53 %, respectively, was performed as described;[9] methyl phenylacetohydroximate was produced, in 42 % yield, by the same procedure. Chromatographic analysis and NMR spectroscopy served to ascertain the stereochemical homogeneity of all three products. On treatment with anhydrous HCl in ether solution, they all underwent stereomutation, and pure specimens of less stabile, higher melting isomers of the two acetohydroximates were isolated. In the phenyl-substituted series, however, the degree of conversion was much lower and separation of the stereoisomers failed. In acetonitrile solution, reconversion to the more stable isomers occurred, with half-lives at 24 °C corresponding to a free energy of activation of about 110 kJ/mol for ethyl and methyl acetohydroximate. In view of the partly conflicting character of the existing data, unambiguous structural assignment became mandatory. An X-ray determination of the higher melting isomer of methyl acetohydroximate proved it to constitute the *Z*-isomer (*3Z*).

X-Ray structure determination. The crystal is built up of layers of molecules, arranged in mirror planes (Fig. 1). In each layer the molecules form cyclic, hydrogen-bonded trimers, with the following dimensions of the hydrogen bond: O···N = 2.787(4) Å, H···N = 1.79 Å and ∠O−H···N = 177°. The molecular packing of the compound is very similar to that of acetoxime,[10] crystallizing in the same space group with similar lengths of the axes. In the

Table 1. Bond lengths (Å) and angles (°).

O1–N2	1.410(4)	O1–N2–C3	112.4(2)
N2–C3	1.274(5)	N2–C3–C4	118.3(3)
C3–C4	1.480(5)	N2–C3–O5	119.8(3)
C3–O5	1.336(3)	C4–C3–O5	121.9(3)
O5–C6	1.441(5)	C3–O5–C6	119.5(3)

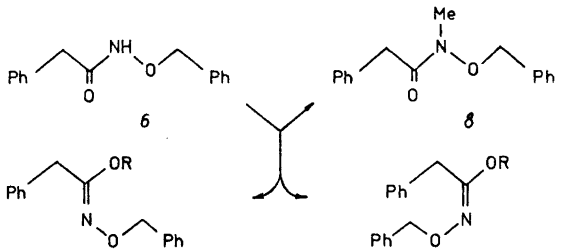
crystal structure of acetoxime only van der Waals forces connect the cyclic, hydrogen-bonded trimers, whereas, in the present structure of methyl *Z*-acetohydroximate, all the hydrogen atoms of the methyl groups are directed toward oxygen atoms of neighbouring molecules, *cf.* Fig. 1. These contacts, with C···H distances of 2.42–2.94 Å, may conceivably define the conformations of the methyl groups and hence contribute to the observed, smaller separation of the layers of trimers (3.418 Å) than in the structure of acetoxime (3.51 Å). The melting point, 126–127 °C, of methyl *Z*-acetohydroximate, when compared with those of the *E*-isomer (28–29 °C) and acetoxime (61 °C), also suggest that strong *inter*-molecular forces are operating in the crystal structure of the former compound.

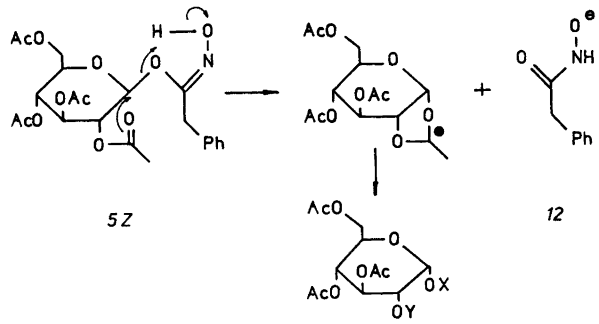
Bond lengths and angles are presented in Table 1, the former agreeing with the corresponding bonds in ethyl *E*- and *Z*-benzohydroximate;[2] some differences were found, however, between corresponding valency angles. In the planar methyl *Z*-acetohydroximate molecule the $O-C_{alkyl}$-bond is situated *antiperiplanar* to the C=N bond. In both isomers of ethyl benzohydroximate these bonds were *synperiplanar*.[2]

Chemical properties. Comparison of melting points, NMR data, and product compositions were utilized in assigning structures to the *2Z/2E* and *4Z/4E* pairs (*vide infra*).

O-Benzyl methyl phenylacetohydroximate, desired as a model for other studies, was produced by methylation of benzyl phenylacetohydroxamate (*6*). The product composition proved highly dependent on the conditions employed; observations, previously made in the aromatic series,[11] were roughly paralleled. Thus, treatment of *6* with diazomethane gave *7Z*, *7E*, and *8*, in the ratio 87:3:10, whereas the silver salt of *6*, on reaction with methyl iodide, yielded the same products, but in the ratio 18:56:26. Assignments (Table 2) were based on ^{1}H NMR characteristics and on the production of *7E* by *O*-benzylation of *4E*. Though stable in benzene solution at 23 °C, the neat *Z*-isomer *7Z* was thermally converted into *7E*, with a half-life of 45 min at 110 °C. In benzene, containing anhydrous HCl, the conversion into *7E* was complete after 2 h at 23 °C. On hydrogenolysis at 20 °C, *7E*, unexceptionally, afforded *4E*, whereas *4Z*, deriving from *7Z*, stereomutated to *4E* in the reaction mixture at a rate only slightly lower than that of the hydrogenolysis reaction.

Extension of the alkylation of *6* to reaction with tetra-*O*-acetyl-α-D-glucopyranosyl bromide furnished, in 75 % yield, an 84:16 mixture of the *O*-benzyl hydroximates *9Z* and *9E* (Table 2), convertible into homogeneous *9E* at 110 °C, with a half-life of 6.3 h, or on standing at 23 °C in HCl-containing benzene, the latter reaction being accompanied, however, by side reactions. Whereas controlled hydrogenolytic debenzylation of *9E* afforded *5E*, *9Z* invariably suffered more deep-seated cleavage, yielding, *inter alia*, 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (*10*),





2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (*11*), and phenylacetohydroxamic acid (*12*), rather than the desired hydroximate *5Z*.

DISCUSSION

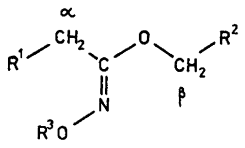
Structural assignments for the products listed in Table 2 rest primarily on (i) consistencies in melting point relations between the pairs of *E*- and *Z*-isomers, (ii) analogies in their NMR spectra, and (iii) the relative stability of the isomers, with reference, in each case, to the authentic (*3Z*/*3E*)-pair.

Within the series of aromatic alkyl hydroximates, the *E*-isomers have melting points higher than those of the *Z*-isomers, a 'rule' which has occassionally been invoked for stereochemical assignments.[5] Apparently, in the present series, the opposite holds true (*cf.* Table 2).

Table 2. ^{1}H NMR shifts of aliphatic hydroximates and some *O*-substituted derivatives.

Compound	M.p. °C	$-CH_2-C-$	$-CH-O-C-$	$-CH_2-O-H$
3Z[a]	126–127[b]	2.00[c]	3.85	
		(1.46)[c]	(3.12)	
3E	21–23[d]	2.00	3.67	
		(1.89)	(3.45)	
2Z	82–84[e]	2.00	4.14	
		(1.56)	(3.63)	
2E	23–24[f]	2.00	3.99	
		(1.90)	(3.90)	
4Z[g]		3.65	3.75	
		(2.93)	(3.27)	
4E	46–47	3.76	3.63	
		(3.74)	(3.36)	
5E	139–140	3.75	5.42	
		(3.10)	(5.47)	
7Z	oil	3.59	3.70	5.05
		(3.28)	(3.35)	(5.04)
7E	oil	3.70	3.62	4.97
		(3.67)	(3.40)	(4.99)
9Z	117–118	3.56	5.39	5.05
		(3.43)	(5.50)	(4.97)
9E	78–79	3.71	5.53	5.05
		(3.53)	(5.58)	(4.97)

[a] X-Ray analysis; present work. [b] Reported:[9] m.p. 123–124 °C. [c] Without parentheses: δ-values in $CDCl_3$; in parentheses: δ-values in C_6H_6. [d] Reported:[9] m.p. 28–29 °C. [e] Reported:[9] 84–85 °C. [f] Reported m.p. 25–26 °C;[6] 22–23 °C.[8] [g] Not isolated in pure form.



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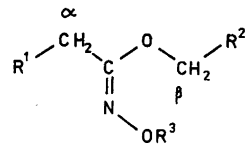

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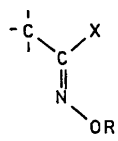
In the ^{1}H NMR spectra of the aliphatic hydroximates a diagnostically useful feature appears to be the stronger deshielding of the α-protons in the *E*-isomers *13*, when measured in deuteriochloroform and/or benzene. Within the class of methyl and ethyl hydroximates, the more deshielded character, in $CDCl_3$-solution, of the β-protons in the *Z*-isomers *14*, paralleled in the aromatic series,[5,12] constitutes another useful structural character (Table 2). Similarly, the ^{13}C spectra are of diagnostic value. Both the α-C and β-C atoms of the *Z*-isomers *14* consistently resonate at lower field than the corresponding nuclei of the *E*-series (*13*). The observed, lower-field absorption of the sp^2-C in the *E*-isomers apparently constitutes an additional feature of diagnostic value (Table 3).

The factors dictating the ease of interconversion and stability of stereometric azomethines are multifarious and frequently subtle. Whereas oximes, *e.g.* (*15*, X = substituted C; R = H or alkyl), appear resistant to uncatalyzed, thermal stereomutation, aromatic *Z*-amidoximes (*15*, X = substituted N; R = H, or CH_2Ph)[13] share with both aromatic [12] and aliphatic alkyl *Z*-hydroximates (*15*, X = substituted O; R = H, alkyl, or benzoyl), the latter reported herein,



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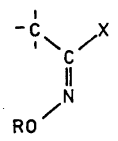

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the propensity to undergo irreversible thermal transformation into the *E*-isomers (*16*). Within the analogous classes of aromatic [14] and aliphatic [15] thiohydroximates (*15*, or *16*, X = substituted S; R = H or CH_3), however, the opposite conversion, *i.e.* that of *16* into *15*, appears to be the favoured process, even when the more stable *Z*-isomers here possess the largest dipole moments.[14]

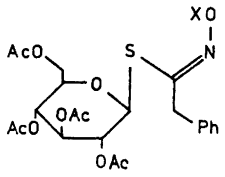
Like in aromatic *O*-alkyl benzohydroximates,[16] amidoximes,[13] and thiohydroximates,[14] the stereomutation of aliphatic hydroximates is considerably facilitated by *N*-protonation, supposedly ascribable, in all cases, to a diminished activation energy for rotation around the C–N-bonds in the protonated species. In the present series, the *Z*/*E*-composition of the protonated equilibrium systems, is highly substituent-dependent, varying from *ca.* 1:3, in the case of *2Z*/*2E* and *3Z*/*3E*, to about 1:9 for *4Z*/*4E*.

The observed, spontaneous fission of the bond between the anomeric carbon and the exocyclic *O*-atom in *5Z*, subsequent to its release from *9Z* on hydrogenolysis, is unparalleled in the *5E*-isomer and deserves comment. Bifunctional, intramolecular general acid and nucleophilic catalysis, as indicated in the formula scheme above, provides a satisfactory explanation for the facility of the reaction and the character of the observed products, *10*, *11* and *12*, and bears resemblance to the mechanism invoked for the facile hydrolysis of 2-carboxyphenyl 2-acetamido-2-deoxy-β-D-glucopyranoside.[17] A control experiment, excluding the participation of cyclic ions, in which the deacetylated analogue of *5Z* was generated upon hydrogenolysis in methanol, yielded, as expected, virtually homogeneous

Table 3. ^{13}C NMR shifts of aliphatic hydroximates and some *O*-substituted derivatives (in $CHCl_3$).

Compound	C_α[a]	C_β[a]	C(sp^2)
3Z	14.0	55.9	155.8
3E	12.7	53.7	163.5
2Z	15.1	64.4	154.9
2E	14.1	62.1	163.0
7Z	35.1	56.6	155.3
7E	33.6	54.0	163.5

[a] For α- and β-designations, see *13* and *14*.



17: X = H
18: X = SO_3^-

methyl α-D-glucopyranoside. In 2-propanol, the corresponding reaction proceeded so much slower that stereomutation of *5Z* into *5E* became the predominant reaction. The observed lability of *5Z* is in obvious contrast to the stability of tetra-*O*-acetyl-β-D-glucopyranosyl phenylacetothiohydroximate (*17*), convertible, *via* tetra-*O*-acetyl benzylglucosinolate (*18*), into benzylglucosinolate,[18] possessing *Z*-configuration, as inferred from its natural relationship to the allylglucosinolate ion, for which X-ray structural evidence exists.[19]

EXPERIMENTAL

Melting points are uncorrected. NMR-spectra were recorded on instruments of the types: Varian-HA-100 (^{1}H) and Bruker WH-90 (^{13}C), mass spectra on a Perkin-Elmer model 270 instrument, and rotations on a Perkin-Elmer 141 polarimeter. Analytical TLC was performed on coated silica gel PF_{254} plates (Merck), with detection in UV, or on spraying with 2 % $FeCl_3$ in 0.1 N hydrochloric acid.

X-Ray structure determination. The crystals used for the X-ray analysis were obtained by diffusion at room temperature of pentane into a solution of the compound in chloroform. Colourless, diamond-shaped crystals were formed.

Crystal data. Methyl *Z*-acetohydroximate, $C_3H_7NO_2$, M = 89.10. Space group $P6_3/m$ (No. 176), $a = 10.913(3)$, $c = 6.837(3)$ Å, $Z = 6$, $D_m = 1.26$ g cm^{-3}, $D_x = 1.26$ g cm^{-3}, $\mu(\mathrm{MoK}\alpha) = 0.75$ cm^{-1}. The unit cell parameters were refined by least-squares techniques from 30 diffractometer-measured θ angles. The crystal density was measured by flotation in a mixture of chlorobenzene and bromobenzene.

Data collection. Three-dimensional diffraction data were measured on a Nonius three-circle automatic diffractometer using the same technique as previously described.[20] All data were obtained from a single crystal with approximate dimensions 0.40 × 0.40 × 0.60 mm. The crystal was sealed in a glass capillary and mounted with [001] along the ϕ axis of the goniostat. Out of the 1332 reflections, ($hk\bar{l}$) and ($\bar{h}k\bar{l}$), measured in the range $2.5 \leq \theta \leq 25°$, 756 had $I_{net} \geq 3.0\sigma(I)$, where $\sigma(I)$ is the standard deviation from counting statistics. These reflections were regarded as observed, whereas the remaining were regarded as unobserved and excluded from the refinement procedure. Lorentz and polarization corrections were applied, but no absorption corrections were made.

Structure determination. The structure was solved by direct methods using the automatic phasing programme *MULTAN*.[21] An *E* map, based on 60 *E*-values with $|E| \geq 2.29$, revealed the positions of the six non-hydrogen atoms. Refinement of the positional and thermal (first isotropic and then anisotropic) parameters of these atoms, using the full-matrix least-squares method, led to an *R*-value of 0.095. The quantity minimized was $\sum w(|F_o| - |F_c|)^2$, where the weights were initially taken as unity. The difference Fourier map showed maxima in positions expected for all the hydrogen atoms of the structure. Introduction of the hydrogen atoms into calculated positions in the refinement as fixed parameters and with isotropic temperature factors set equal to those of the atoms to which they are bonded, led to a final *R*-value of 0.063 for all observed reflections. The weighting scheme used in the last cycles of refinement was of the form $w = 1/(1 + [(|F_o| - 7.5)/7.5]^2)$. Tables 4 and 5 list the final positional and thermal parameters for the non-hydrogen atoms, and hydrogen atoms, respectively. The final list of structure factors is available from one of the authors (I.K.L.) on request. All atoms within the molecule show large thermal motion in the *z* direction, *cf.* Table 4. As a test of the planarity of the molecule the atoms were allowed to move out of the mirror plane by least-squares refinement of the structure in the acentric space group $P6_3$. But the shifts of the atoms out of the plane were not significant, and the vibration of the atoms in the *z* direction were still large. Accordingly, the parameters from the refinement in the centrosymmetric space in group $P6_3/m$ were chosen as the final parameters. The programmes used in the crystallographic analysis were the same as those previously employed.[20] The X-ray atomic scattering factors used for hydrogen were those of Stewart, Davidson and Simpson,[22] and for oxygen, nitrogen and carbon those of Cromer and Mann.[23]

Methyl and ethyl E-*acetohydroximate* (3E) *and* (2E). The two esters were prepared from methyl and ethyl acetimidate hydrochloride and hydroxylamine hydrochloride, essentially as described in the patent literature.[9] NMR: *cf.* Tables 2 and 3.

Methyl E-*phenylacetohydroximate* (4E). Application of the same conditions to the reaction between methyl phenylacetimidate and hydroxylamine gave, after recrystallization from light petroleum, the expected ester (42 %), m.p. 42 – 45 °C. An analytical specimen was produced by repeated sublimation at 10^{-5} mmHg (bath

Table 4. Final positional and thermal parameters ($\times 10^3$) for the non-hydrogen atoms. The temperature factors are defined by: exp $[-2\pi^2 (U_{11}h^2a^{*2} + \cdots + 2U_{12}hka^*b^* + \cdots)]$.

Atom	x/a	y/b	z/c	U11	U22	U33	U12	U13	U23
O1	.4360(2)	.1809(2)	.2500	4.0(1)	4.3(1)	13.1(3)	2.6(1)	.0	.0
N2	.4756(3)	.3254(3)	.2500	3.5(2)	3.7(1)	9.1(3)	1.5(1)	.0	.0
C3	.3690(3)	.3435(3)	.2500	3.5(2)	3.9(2)	6.0(3)	1.7(1)	.0	.0
C4	.3948(4)	.4901(3)	.2500	5.4(2)	4.2(2)	11.3(3)	2.4(2)	.0	.0
O5	.2384(2)	.2315(2)	.2500	3.0(1)	4.0(1)	11.4(2)	1.7(1)	.0	.0
C6	.1183(3)	.2527(4)	.2500	4.1(2)	6.7(2)	11.0(4)	3.2(2)	.0	.0

40 °C), m.p. 46 – 47 °C. Anal. $C_9H_{11}NO_2$: C, H, N. ^{1}H NMR: *cf.* Table 2.

Methyl and ethyl Z-acetohydroximate (3Z) and (2Z). Partial stereomutation of the two *E*-esters was achieved by means of ethereal hydrogen chloride, essentially as described.[9] Selective extraction of unchanged *E*-esters with light petroleum facilitated the purification of the *Z*-isomers. *3Z:* Yield 19 % (recovered 28 % of the *E*-isomer), m.p. 126 – 127 °C (from $CHCl_3$: hexane), specimen for X-ray analysis. ^{1}H and ^{13}C NMR: *cf.* Tables 2 and 3. *2Z*: Yield 21 % (recovered 52 % of the *E*-isomer), m.p. 82 – 84 °C (84 – 85 °C [9]). ^{1}H and ^{13}C NMR: *cf.* Tables 2 and 3.

O-Benzyl phenylacetohydroxamate (6). Ethyl phenylacetate was converted into phenylacetohydroxamic acid (yield 63 %, m.p. 140 – 142 °C) by the method described for the preparation of benzohydroxamic acid.[24] *O*-Benzylation of the hydroxamic acid was performed, following the directions given for the synthesis of *O*-alkylated benzohydroxamic acids.[25]

O-Benzyl phenylacetohydroxamate (*6*) was obtained in 79 % yield, m.p. 77 – 79 °C (Lit.[26] 78 – 80 °C): ^{1}H NMR: δ 3.47 (2 H, br.s), 4.83 (2 H, s), 7.25 (5 H, s), 7.41 (5 H, s), 8.32 (1 H, br.s).

Methylation of O-benzyl phenylacetohydroxamate (6). (a) *With diazomethane.* A solution of *6* (4 mmol) in ether (4 ml) and methanol (1 ml) was treated, for 3 days at 22 °C, with a large excess of ethereal diazomethane. Estimated by ^{1}H NMR, the reaction mixture contained the *Z-O*-methyl (*7Z*), *E-O*-methyl (*7E*), and *N*-methyl (*8*) derivatives in the ratio 87:3:10. Preparative TLC, with benzene:ethyl acetate (9:1) as an eluent, afforded the major constituent (yield 69 %), R_F 0.65, consisting of methyl *Z-O*-benzyl phenylacetohydroximate (*7Z*), as a colourless oil, short-way distilled (10^{-5} mmHg, 80 °C) before analysis, n_D^{25} 1.5628. Anal. $C_{16}H_{17}NO_2$: C, H, N. ^{1}H and ^{13}C NMR: *cf.* Tables 2 and 3. MS [IP 70 eV; *m/e* (% rel.int.)]: 256 (25), 255 (90, M), 239 (10), 238 (50), 164 (10), 132 (49), 117 (10), 107 (15), 106 (10), 105 (40), 104 (23), 92 (60), 91 (100), 90 (15), 89 (20), 79 (10), 78 (10), 77 (41), 65 (74), 63 (10), 51 (29), 39 (24), 32 (25), and 28 (90).

With methyl iodide. The silver salt of (*6*) (4 mmol), prepared as described for a similar salt,[5] was suspended in ether (2 ml) and stirred for 40 h at 22 °C in the dark with methyl iodide (8 mmol). The oily reaction product (1.1 g), estimated, by ^{1}H NMR, to contain *7Z*, *7E*, and *8* in the ratio 18:56:26, was separated into three fractions on silica gel plates, with benzene ethyl acetate (9:1) as the solvent. The fastest moving band (R_F 0.9) (49 %) contained methyl *E-O*-benzyl phenylacetohydroximate (*7E*), purified by short-way distillation (10^{-5} mmHg, 75 °C), n_D^{25} 1.5512. Anal. $C_{16}H_{17}NO_2$: C, H, N. ^{1}H and ^{13}C NMR: *cf.* Tables 2 and 3. The MS was indistinguishable from that of *7Z*. The second band (R_F 0.7) contained *7Z* (14 %), identical with the material described above; from the slowest moving band (R_F 0.5) was obtained a 16 % yield of benzyl *N*-methylphenylacetohydroxamate (*8*), distilled at 10^{-5} mmHg (75 °C) before analysis. n_D^{25} 1.5630. Anal. $C_{16}H_{17}NO_2$: C, H, N. ^{1}H NMR: 3.20 (3H, s), 3.69 (2H, s), 4.75 (2H, s), 7.23 (5H, s), and 7.35 (5H, s). MS [IP 70eV; *m/e* (% rel.int.)]: 255 (14, M), 210 (15), 209 (90), 208 (36), 181 (20), 105 (10), 92 (85), 91 (100), 90 (15), 89 (20), 77 (30), 65 (85), 63 (15), 51 (20), 39 (30), 32 (30), and 28 (80).

O-Benzylation of 4E. A methanol solution (40 ml), containing sodium methoxide (30 mmol), methyl *E*-phenylacetohydroximate (*4E*) (30 mmol), and benzyl bromide (30 mmol), was refluxed for 2 h. After evaporation to dryness and extraction with chloroform, the residual oil was fractionally distilled at 11 mmHg to

Table 5. Positional and thermal parameters used for the hydrogen atoms.

Atom	x/a	y/b	z/c	B
H1	.519	.166	.250	3.7
H41	.345	.500	.131	4.5
H42	.491	.575	.250	4.5
H61	.127	.312	.131	3.8
H62	.020	.171	.250	3.8

give benzyl methyl ether (b.p. 57 – 59 °C) (1.1 g) and a higher-boiling fraction (b.p. 140 – 190 °C), consisting, according to ^{1}H NMR analysis, of about equal amounts of starting material (*4E*) and the *O*-benzyl derivative (*7E*). The latter was separated from other constituents by column chromatography on silica gel (200 g), with chloroform as the eluent. A 36 % yield was obtained of a colourless oil, identified, by n_D^{25} and ^{1}H NMR, as *7E*.

Hydrogenolysis of 7E *and* 7Z. Methyl *E*-*O*-benzyl phenylacetohydroximate (*7E*) (1.1 mmol) was dissolved in ethyl acetate (10 ml). 5 % Palladium on charcoal (250 mg) was added, and the mixture was shaken with hydrogen (3 at) at 22 °C for 2 h. After filtration and evaporation, an oil remained which, according to TLC and ^{1}H NMR, consisted of homogeneous *4E*. Subjecting the isomeric *Z*-*O*-benzyl methyl ester (*7Z*) to the same reaction conditions resulted in the production, after only 1 h, of a *ca.* 78:22 *E*/*Z*-ratio of the debenzylated species, with only traces present of the starting material. Prolonged reaction times gave more complicated mixtures. Performing the reaction in tetrahydrofuran and ether, or changing the catalyst to palladium oxide or palladium on barium sulfate, resulted in no improvement. On rapid and cautious TLC (benzene:ethyl acetate, 4:1), a colourless oil (12 %) was obtained and identified as methyl *Z*-phenylacetohydroximate (*4Z*) on the basis of ^{1}H NMR data (*cf.* Table 2). Attempts at further purification invariably resulted in its stereomutation to *4E*.

Tetra-O-*acetyl*-*β*-D-*glucopyranosyl*-Z-O-*benzyl phenylacetohydroximate* (9Z). A suspension of the silver salt of *O*-benzyl phenylacetohydroxamic acid (*6*) (15.5 mmol), drierite (5 g), and tetra-*O*-acetyl-α-D-glucopyranosyl bromide (14 mmol) in acetonitrile (40 ml) was stirred, in the dark, for 64 h at 22 °C. After filtration and evaporation, the reaction mixture was separated by preparative TLC on silica gel plates (benzene:ethyl acetate, 4:1) into a major (R_F 0.5), and a minor (R_F 0.6) product. The former was recrystallized from ethyl acetate: light petroleum to give a colourless product, m.p. 116 – 118 °C. An analytical specimen was produced by additional recrystallizations from the same solvent and aqueous methanol, m.p. 117 – 118 °C, $[\alpha]_D^{25}$ – 3.9° (*c* 1.0, chloroform). Anal. $C_{39}H_{33}NO_{11}$: C, H, N. By ^{1}H NMR spectroscopy, the product was assigned the *Z*-configuration *9Z*, *cf.* Table 2. The minor product, undoubtedly representing the *9E*-isomer, could be more conveniently isolated after treating the original glucoside-mixture (6.7 g) in benzene solution (40 ml) with HCl-saturated benzene (1 ml) for 20 h at 22 °C. After column chromatography [silica gel (200 g), chloroform:ethyl acetate (4:1)], the *E*-glucoside (*9E*, 3.2 g), m.p. 71 – 73 °C was obtained in virtually homogeneous form. An analytical specimen, m.p. 78 – 78.5 °C, was produced by two recrystallizations from ethyl acetate:light petroleum, $[\alpha]_D^{20}$ – 88.4 °C (*c* 1.0, chloroform). Anal. $C_{29}H_{33}NO_{11}$: C, H, N. ^{1}H NMR: *cf.* Table 2.

Hydrogenolysis of 9E *and* 9Z. Subjected to hydrogenolysis, as described above, the *O*-benzylated *E*-glucoside *9E* afforded, after 18 h, a mixture of compounds, which was separated by preparative TLC on silica gel plates, with chloroform:ethyl acetate (2:1) as a solvent, into starting material (R_F 0.7, 12 %), the expected, debenzylated glucoside tetraacetate (*5E*, R_F 0.4, 50 %), an oily material (R_F 0.2, 30 %), exhibiting an ^{1}H NMR spectrum in keeping with its identity as 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (*11*), admixed with traces of the 1,3,4,6-isomer (*10*),[27] and, finally, phenylacetamide (R_F 0.1, 18 %). Benzyl alcohol was not detected, and it was ascertained that the major product (R_F 0.4), when subjected to the hydrogenolysis conditions, did, in fact, undergo fission into phenylacetamide, *10* and *11*. Repeated recrystallizations of the major product from ethyl acetate:light petroleum gave an analytical specimen of *5E*, m.p. 139 – 140 °C, $[\alpha]_D^{20}$ – 91° (*c* 1.0, chloroform). Anal. $C_{22}H_{27}NO_{11}$: C, H, N. For ^{1}H NMR data, *cf.* Table 2. When the *Z*-isomer *9Z* was similarly treated, preparative chromatography of the reaction mixture, after 5 h, when no starting material was left, afforded the tetraacetates *11* and *10*, in addition to phenylacetohydroxamic acid (*12*), contaminated with traces of phenylacetamide, the latter shown to be slowly formed from *12* under the conditions employed. All attempts to conduct the reaction so that *5Z* could be isolated proved of no avail.

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