aliphatic glyoxyloyl chlorides appear [4] to decarbonylate *via* a radical chain.

Experimental. General. Mass spectra and IR spectra were recorded on an LKB-9000 and a Perkin-Elmer 421 spectrometer, respectively. Gas chromatographic separations were carried out at 50 °C using a 1.8 m × 3 mm column packed with molecular sieves (5A). ^{18}O enriched H_2O with a content of 20 % and 40 % ^{18}O was used.

Indole-3-glyoxyloyl chloride 3 was prepared from indole and oxalyl chloride according to Speeter and Anthony.[5]

4a. 3 (207 mg, 1 mmol) was hydrolysed by ^{18}O enriched H_2O (19 μl) in THF (1 ml) at 0 °C. After 1 min the solvent was rapidly evaporated *in vacuo*. The produced indole-3-glyoxalic acid [m.p. 218 °C (acetonitrile) lit.[6] 216 °C] was analysed for its ^{18}O content by mass spectrometry.

4b. Indole-3-glyoxylic acid (unlabelled, 189 mg) ^{18}O enriched H_2O (92 μl) and 8 μl conc. HCl was stirred in THF (1 ml) for 24 h at room temperature. After the reaction was completed the solvent was removed *in vacuo* and the acid analysed for its ^{18}O content (*MS*).

3a and *3b*. The appropriate labelled indole-3-glyoxylic acid *4a* or *4b* (189 mg) was treated with $SOCl_2$ (250 μl) in a mixture of THF (3 ml) and ether (2 ml) for 20 h at room temperature. After this time the solvent and excess $SOCl_2$ were removed *in vacuo*.

Decarbonylation of 3a *and* 3b was performed at 120 °C as described in Ref. 3, using diglyme or tetrachloroethane as solvent.

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Chemical Synthesis and Disproportionation of *N*-Hydroxytyrosine

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In spite of the various routes reported for the chemical synthesis of *N*-hydroxyamino acids [1–3] they remain difficult to obtain either because of instability, poor yields, or limited applicability of each of the methods. *N*-Hydroxyamino acids have been established as components of several naturally occurring compounds [4,5] and have also, although the experimental data are weak, been postulated to be involved in the biosynthesis of several classes of secondary plant products.[6] We were particularly interested in testing *N*-hydroxytyrosine as an intermediate in the biosynthesis of the cyanogenic glucoside dhurrin and this report describes its synthesis and characterization.

Experimental. N-Hydroxytyrosine was synthesized by a modification of the method described by Ahmad.[3] *p*-Hydroxyphenylpyruvic acid (20 mmol) and hydroxylamine hydrochloride (30 mmol) were dissolved in a mixture of 35 ml of H_2O, 25 ml of EtOH and 45 ml of 1 M NaOH. Sodium cyanoborohydride (35 mmol) was added and pH kept at 4 by the addition of 1 M HCl. After reaction at room temperature for 24 h an additional 35 mmol of sodiumcyanoborohydride were added. After 60 h the reaction was stopped by the addition of concentrated HCl to pH ~0. The reaction mixture was evaporated to dryness at 30 °C in a rotary evaporator. The yellow residue was suspended in 50 ml of EtOH and insoluble inorganic material removed by filtration. The ethanol extract was evaporated to dryness and analytically pure *N*-hydroxytyrosine was obtained as white crystals in 74 % yield by recrystallizing the residue from hot water (Found: C 54.64; H 5.70; N 7.11. Calc. for $C_9H_{11}NO_4$: C 54.82; H 5.62; N 7.10). M.p. 226–228 °C (decomp.). MS [IP 70 eV, solid probe, 140 °C]: 197 (M^+), 107 (base peak). Potentiometric titration: $pK_1 = 2.52$ and $pK_2 = 5.26$.

Results and discussion. N-Hydroxyamino acids described earlier have shown considerable discrepancies in both physical and chemical properties.[3] The main criteria used for identification and purity has been elemental analysis, providing only little information on the nature of the impurities present. In this study NMR analysis was found very suitable for analyzing

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Table 1. Chemical shifts of *N*-hydroxytyrosine and related compounds.

	δ
N-Hydroxytyrosine	6.77 and 7.11 (2 doublets, 4 arom. H, J ~8 Hz), 4.26 (d of d, 1 H, J ~6 Hz), 3.20 (m) [a]
Tyrosine	6.79 and 7.14 (2 doublets, 4 arom. H, J ~8 Hz), 4.08 (app. t., 1 H, J ~6 Hz), 3.18 (m) [a]
p-Hydroxyphenylpyruvic acid oxime	6.63 and 7.06 (2 doublets, 4 arom. H, J ~8 Hz), 3.76 (s, 1 H)
p-Hydroxyphenylacetaldoxime	6.69 and 7.03 (2 doublets, 4 arom. H, J ~8 Hz), 6.74 (5, 1 H, J ~5), 3.56 (d, 2 H, J ~5)

[a] Overlaps HCD_2OD signal.

reaction mixtures and products obtained (Table 1). Smaller quantities of *N*-hydroxytyrosine and possible contaminants are best analyzed by gas chromatographic separation of their trimethylsilyl derivatives as recently described.[7] These two analytical methods were extensively used during this study and should have rather general applicability. The recrystallized *N*-hydroxytyrosine sample obtained contained no impurities when analyzed by either of these two methods. The yields obtained by the unmodified method of Ahmad [3] involving reduction at higher pH for a shorter time period were much lower (30–40 %) and the product obtained difficult to purify because of incomplete reduction of *p*-hydroxyphenylpyruvic acid oxime under these conditions. When the reaction mixture subsequently was acidified, this compound decomposed resulting in the requirement of additional purification steps *via* ion exchange chromatography.

When refluxed under nitrogen, α-*N*-hydroxyamino acids are reported to disproportionate to the corresponding α-amino acid and α-ketoacid oxime.[8] Although phenylpyruvic acid oxime has been isolated in low yield as a disproportionation product of *N*-hydroxyphenylalanine, the assumption of the involvement of an α-ketoacid oxime in this disproportionation reaction of *N*-hydroxyamino acids is generally based on the formation of equimolar amounts of α-amino acid and carbon dioxide. The latter is assumed to be formed from the rapid conversion of the α-ketoacid oxime to the homologous lower nitrile.[8] However, when *N*-hydroxytyrosine was refluxed under nitrogen, equimolar quantities of tyrosine and *p*-hydroxyphenylacetaldoxime were formed with only traces of *p*-hydroxyphenylacetonitrile and no *p*-hydroxyphenylpyruvic acid oxime present. Reflux of *p*-hydroxyphenylacetaldoxime [9] resulted in a similar small amount of *p*-hydroxyphenylacetonitrile while reflux of *p*-hydroxyphenylpyruvic acid oxime resulted in nearly complete conversion to *p*-hydroxyphenylacetonitrile. It is therefore concluded that *p*-hydroxyphenylpyruvic acid oxime is not an intermediate in the disproportionation of *N*-hydroxytyrosine and the earlier postulated involvement of α-ketoacid oximes in the disproportionation of *N*-hydroxyamino acids when refluxed under nitrogen based solely on carbon dioxide production [8] thus would appear to be questionable.

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