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SELECTIVE MONODEOXYGENATION OF QUINOXALINE-AMINO ACID AND ESTER DIOXIDES

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Abstract—Trimethyl phosphite selectively removes the N-1-oxygen in N-(3-methyl-2-quinoxaloyl) L-α-amino ester-1,4-dioxides, whereas it removes the N-4-oxygen in the corresponding series of dioxides lacking the C_3-Me. This selectivity reversal reflects the relative strength of the intrahydrogen-bridging to the N-1-oxygen. The monoxides having the favourable N-oxygen are not reduced to the quinoxalines, implying that the reagent requires doubling of the N-oxide function for deoxygenation. However, alkaline sodium dithionite removes the N-1-oxygen in both series of the amino acid-dioxides, as well as in the parent quinoxaline-2-carboxylic acid-dioxides, a result that contradicts the report stating removal of the N-4-oxygen. The N-oxygenated quinoxalinium ion (*m/e* 145 or 159) prevails in the MS of the 4-oxides, but it is not observed (<1%) for the isomeric 1-oxides. ^{1}H NMR, ^{13}C NMR and UV spectral data also offer diagnostic criteria for differentiation between the isomeric 1- and 4-oxides. Aryl-heteryl "interaction" (as revealed by ^{1}H NMR, though not by ^{13}C NMR in the aromatic amino ester dioxides) is not manifested in the corresponding monoxides.

Recently, we have reported on N-(3-methyl-2-quinoxaloyl) L-α-amino acid and ester dioxides (3 and 7) and their non-oxygenated analogues (**1a–d**, **2a–d**).[1,2] We now extend our studies to the corresponding amino ester monoxides **5a–d**, **9a–d**, and the nor C_3-Me analogues **6a–d**, **10a–d**, with emphasis on the observed selective deoxygenation of the parent dioxides.

Synthesis. Deoxygenation of quinoxaline dioxides by various reagents often yield mixtures of the corresponding monoxides together with the non-oxygenated quinoxalines. Selective monodeoxygenation of certain quinoxaline dioxides has been reported using alkaline sodium dithionite,[4] and trimethyl phosphite.[5] The phosphite removes the N-1-oxygen in methyl 3-methylquinoxaline-2-carboxylate-1, 4-dioxide (**13b**),[5] whereas the dithionite was claimed to remove the N-4-oxygen in quinoxaline-2-carboxylic acid 1,4-dioxide (**14a**).[4] In the present work, both reagents were utilized to prepare the quinoxaline-amino ester monoxides **5**, **6**, **9** and **10a–d** from the corresponding dioxides **3**, **4**, **7** and **8a–d** (Scheme 1). The N-1 or N-4-oxide assignments were established by chemical transformations, coupled with sound spectroscopic data. Our results reveal that dithionite always removes preferentially the N-1-oxygen (next to the electron-withdrawing group) rather than the N-4-oxygen as reported previously.[4] On the other hand, trimethyl phosphite can remove selectively either the N-1 or the N-4-oxygen, depending on the extent of stabilizing interactions involving the N-1-oxygen and the nearby amide substituent.

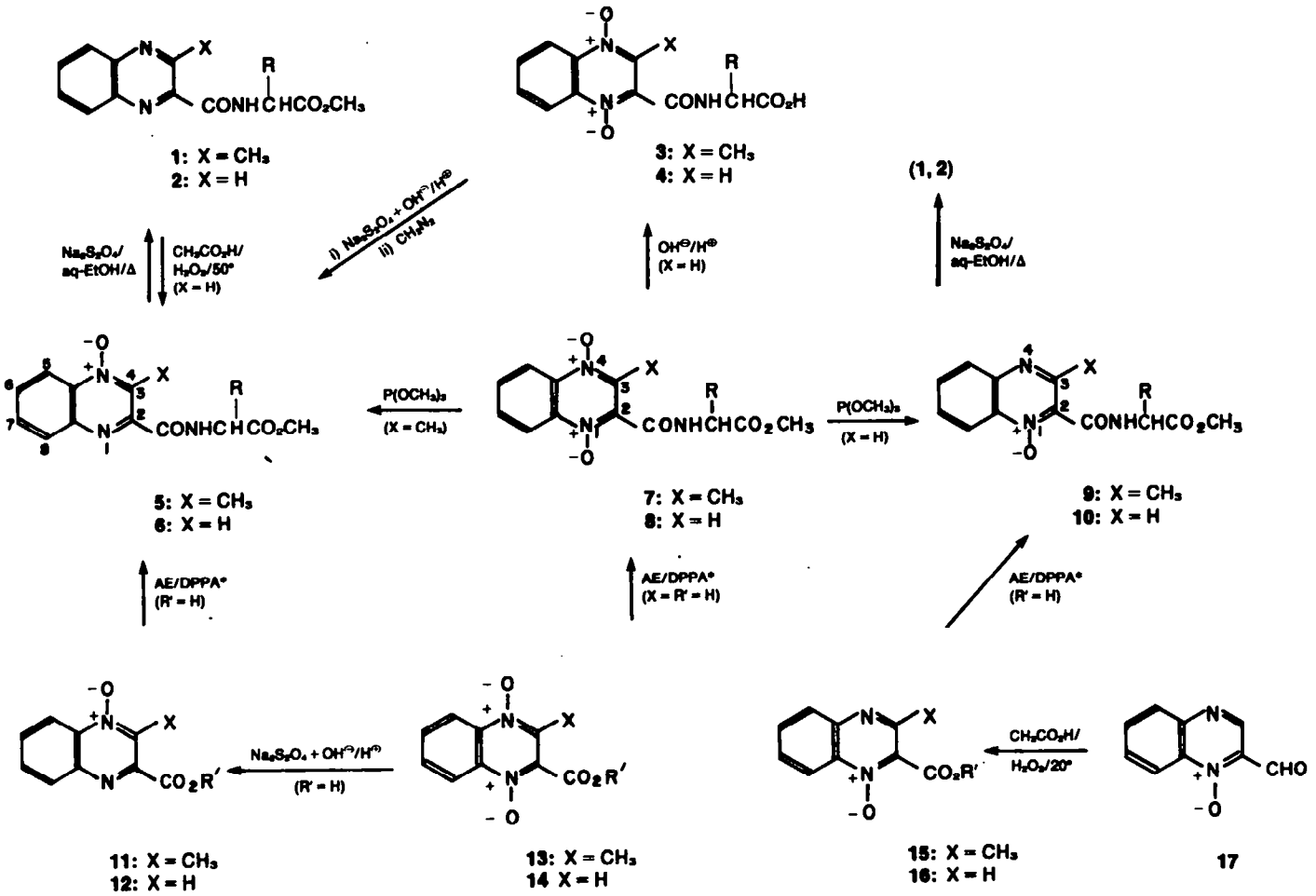
Sodium dithionite. The quinoxaline-2-carboxylic acid monoxide (obtained by alkaline dithionite-reduction of the parent dioxide **14a**) has different physical and spectral properties from those of quinoxaline 2-carboxylic acid-1-oxide of known structure **16a**,[a] but it is identical in every respect with an authentic sample of the isomeric 4-oxide **12a**.[b] Similarly, the alkaline dithionite-reduction of 3-methyl-quinoxaline-2-carboxylic acid-1,4-dioxide (**13a**) gives the corresponding 4-oxide **11a** which is identical with an authentic sample.[5] The reagent also deoxygenates the N-1-oxygen nearest to the 2-carboxamido group in dioxides **3a–d** and **4a–d**, and leads to the production of the corresponding 4-monoxides (characterized by conversion to their methyl esters **5a–d** and **6a–d**, respectively). The N-4-oxide assignment is confirmed by their having identical properties to those obtained by DPPA-coupling of the particular amino ester with the respective quinoxaline-2-carboxylic acid-4-oxides **11a** and **12a** (Scheme 1). This coupling reaction is also adopted for the synthesis of the isomeric amide-1-oxides **9a–d** and **10a–d** utilizing the parent quinoxaline-2-carboxylic acid-1-oxides **15a**, **16a**, respectively (Scheme 1) (**15a** is obtained from the corresponding ester **15b**[5] by mild saponification).

These results contradict a literature report[4] claiming the preferential loss of the N-4-oxygen from dioxide **14a**, but are in agreement with a mechanism recently suggested[7] for dithionite-reduction whereby the dithionite anion hooks preferentially to the more electrophilic hetero ring carbon (C_2) carrying the electron-withdrawing carboxylate or carboxamido substituents, with subsequent removal of the nearby N-1-oxygen.

Trimethyl phosphite. This reagent selectively removes

[a] Prepared in this study from quinoxaline-2-carboxaldehyde 1-oxide (**17**)[5] by peracetic acid oxidation (Scheme 1).

[b] Obtained by saponification of the corresponding ester **12b** prepared in turn, by preferential N-4-peroxidation of methyl quinoxaline-2-carboxylate.[4]



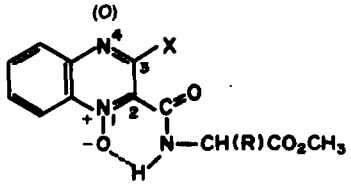
Compds 1–10	a	b	c	d
R	Me	$CHMe_2$	Ph	$PhCH_2$

Compds 11–16	a	b
R'	H	Me

*AE = L-α-amino acid methyl ester hydrochloride; DPPA = diphenylphosphoryl azide

Scheme 1.

the N-1-oxygen in amides **7a–d**, in accord with its behaviour towards the carboxylate ester[c] **13b**[5] (Scheme 1). It is interesting to note that the selectivity of this reagent is *reversed* in the corresponding amides **8a–d** lacking the C_3-Me group where the N-1-oxygen is retained in the products **10a–d**. This is confirmed by their identity with those obtained via the DPPA-coupling[6] of quinoxaline-2-carboxylic acid-1-oxide (**16a**) with the particular amino ester (Scheme 1). This *selectivity reversal* might be attributed to the presence of stronger intramolecular hydrogen-bonding between the N-1-oxygen and the amide-NH compared to the C_3-Me analogues represented in Ia and Ib, respectively. ^{1}H NMR spectral data give credibility to this explanation [δNH *ca.*[d]



I: oxygenated N_4; II: non-oxygenated N_4
(a: X = H; b: X = CH_3)

9.0 ppm for **7** (Ia), and 11.0 ppm for **8**(Ib); also the rate of the amide-NH exchange with deuterium oxide is rather slow in **7** (25% exchange after 16 hr at 20°) compared to that of **8** (80% exchange after 0.5 hr at 20°)]. This decrease in the hydrogen-bridging strength in Ib might be attributed to the *ortho*-effect of the C_3-Me group which forces the amide CO slightly out of the plane of the heteraromatic ring. Similar effects on the coplanarity of the CO have been observed in *o*-toluamides and related systems.[8]

It seems likely that deoxygenation by trimethyl phosphite involves initial bonding between the P atom and an N-oxygen.[9] In the dioxides **8a–d** this bonding occurs preferentially at the more available N-4-oxygen, the N-1-oxygen being tied up by intrahydrogen-bridging.

Representative quinoxaline-1-oxides (**9a** and **15b**) and 4-oxides (**6a** and **6c**) were subjected to the action of trimethyl phosphite under the conditions specified for the corresponding dioxides. No deoxygenation to the corresponding quinoxalines was detected, and the monoxides were recovered unchanged. This implies that, in a way, the presence of both N-oxide functions is essential for successful deoxygenation by this reagent.

Optical purity. The reagents and experimental conditions, employed in the preparation of the chiral quinoxaline-amino ester monoxides (**5**, **6**, **9** and **10a–d**), are expected to avoid racemization. This was ascertained by complete deoxygenation, using excess dithionite in refluxing aqueous ethanol,[2,7] of representative quinoxaline monoxides (**5d**, **9d**), (**9a**), (**6a**, **10a**) and (**6c**) to the corresponding quinoxalines **1d**, **1a**, **2a** and **2c**, respectively. In all cases the product was found to have almost the same specific rotation as that of an optically pure (>95%) authentic sample.[3]

Spectral characterization. NMR, UV and MS spectral data are applied here to differentiate between the isomeric 1- and 4-oxides.

^{1}H NMR spectra. The criteria employed to differentiate the isomeric monoxides **5a–d** and **9a–d** are the aromatic multiplicity pattern, the -NH and the C_3-Me chemical shifts. The multiplicity pattern of the H_5–H_8 aromatic protons in the 1-oxides **9a–d** (two multiplets, 1:3) is different from that of the corresponding 4-oxides, **5a–d** (three multiplets 1:1:2), and differentiates both monoxides from either the quinoxalines or their dioxides (each, two multiplets, 2:2). In the 1-oxide series **9a–d** the NH proton is, as expected, more deshielded (9.0 ppm) whereas the C_3-Me protons are surprisingly more shielded (2.7 ppm) when compared to those of the corresponding 4-oxides **5a–d** (8.55 and 3.00 ppm, respectively). The increased shielding of the C_3-Me protons in the 1-oxides is probably the result of an imposed conformational arrangement similar to Ib. In this arrangement, the CO group is forced slightly out of plane and points towards the C_3-Me group which falls under the direct influence (anistropic field) of the CO group. Noteworthy is that the chemical shift of the C_3-Me protons is almost the same in both aliphatic (**9a**, **9b**) and aromatic (**9c**, **9d**) amino ester 1-oxides.[e] This behaviour is different from that of the corresponding 1,4-dioxides in which aryl-heteryl "interaction" in the aromatic amino ester dioxides leads to a shielding effect (*ca.* 0.2 ppm) compared to the aliphatic counterparts.[2] It seems, therefore, reasonable to assume that both oxide functions are essential in order to observe this shielding effect of the aryl moiety of the aromatic amino ester residue.

The N–H and the C_3–H protons are more deshielded in the 1-oxides **10** (δ 10.95 and 9.60 ppm, respectively) than in the corresponding 4-oxides **6** (δ 8.50 and 9.05 ppm, respectively).[f] The chemical shifts of the C_3–H proton in the aliphatic (**8a**, **8b**) and aromatic (**8c**, **8d**) amino ester dioxides (δ 9.12 and 9.04 ppm, respectively) differ by *ca.* 0.08 ppm. Such a difference, though small, is not observed in the corresponding 1-oxides **10a–d**.[e] Once more, it appears here that both N-oxide functions are required in order to promote aryl-heteryl "interaction".

^{13}C NMR spectra. In general, the introduction of an N-oxide oxygen exerts a shielding effect on the nearby carbons to a varying degree. In particular, the C_3–CH_3 carbon chemical shifts in the 4-oxides **5a–d** (δ 141.8 and 13.6 ppm, respectively) are smaller than those in the corresponding 1-oxides **9a–d** (δ 155.9 and 24.3 ppm, respectively). Also, the C_2 and the amide CO carbons have lower δ values in the 1-oxides **9a–d** (133.2 and 160.7 ppm, respectively) than in the 4-oxides **5a–d** (145.8 and 163.6 ppm, respectively). Comparable trends for the C_3, C_2 and CO-amide carbon chemical shifts are also observed in the corresponding isomeric monoxides **6a–d** and **10a–d** lacking the C_3–Me group. It is interesting to note that the chemical shifts of the C_3–CH_3 carbon in the dioxides **7a–d** (*ca.* 14.4 ppm) is invariant to the nature of

[c] We find that the selectivity of this reagent is less pronounced in the 2-carboxylate dioxide **14b** lacking the C_3-methyl group where both the 1-oxide **16b** and the 4-oxide **12b** together with unchanged **14b** are obtained in the ratios 1:3:6, respectively (as evident from the integrated peak area of the C_3–H proton signals at 9.08, 9.03 and 8.66 ppm, respectively). The results demonstrate that selectivity is governed by a delicate balance between steric and electronic effects of which the latter prevails.

[d] Center of doublet; **7c** and **8c** show exceptionally higher δ values (9.7 and 12.1 ppm, respectively) due to the added inductive effect of the phenyl group (R).

[e] The isomeric 4-oxides behave similarly.

[f] Higher δ values, observed for the N–H proton in **10c** and **6c** (12.11 and 8.92 ppm, respectively), are attributable to extra deshielding inductive effect of the phenyl group.

the (R) group (aliphatic or aromatic). This is in contrast to the shielding influence on the C_3–Me protons exerted by the sidechain aromatic (R) group in these dioxides.[2] Except for the electronic N-oxide effect, no other effects attributed to special conformational arrangements were detected, as was the case in ^1H NMR. Detailed ^{13}C NMR assignments on these systems will be communicated separately.

UV spectra. The $\pi \rightarrow \pi^*$ transitions in the 4-oxides (**5**, **6a–d**) show a sizable (5–7 nm) blue-shift in going from nonpolar (cyclohexane) to polar protic solvents (ethanol). This is a characteristic behaviour of the aza-aromatic N-oxides,[10] and is attributed to solute–solvent interactions (mainly intermolecular hydrogen-bonding). However, in the 1-oxides (**9**, **10a–d**) these $\pi \rightarrow \pi^*$ bands, especially those located at longest wavelengths, are insensitive to changes in solvent polarity in **10a–d** (Fig. 1) and only slightly blue shifted in **9a–d**. This behaviour might be the result of the intramolecular H-bonding which is strong enough in **10a–d** to exclude the possibility of interhydrogen-bridging of the N-1-oxygen with ethanol.

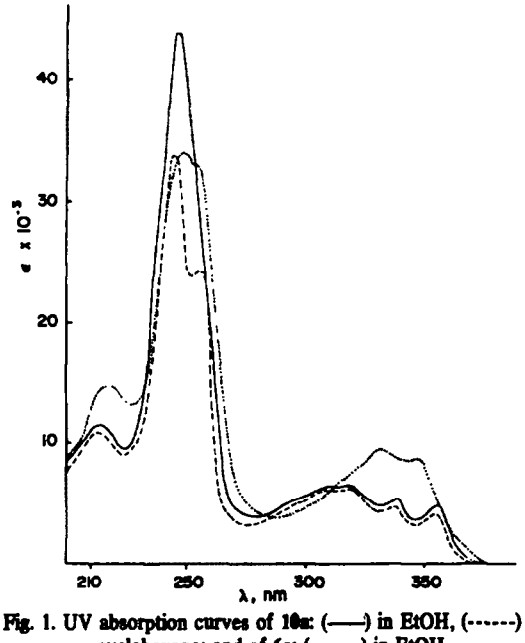


Fig. 1. UV absorption curves of **10a**: (——) in EtOH, (------) in cyclohexane: and of **6a**: (. . . . .) in EtOH.

Mass spectra. A striking difference between the mass spectra of the 4-oxides **5a–d**, **6a–d**, **11b** and **12b** and their isomeric 1-oxides **9a–d**, **10a–d**, **15b** and **16b** lies in the fragment ions IV and V (Scheme 2). The former N-oxygenated quinoxalinium ion IV *predominates* in the spectra of the 4-oxides (base peak in few cases), whereas the latter quinoxalinium ion V predominates in the spectra of the 1-oxides, and is the base peak. The oxygenated ion IV is *not observed* (<1%) in the spectra of the 1-oxides (a result of the difficulty of placing two positive charges on adjacent atoms), the deoxygenated ion V being produced in a one-step expulsion of CO_2 from ion III as confirmed by the corresponding metastable peak (Ion III is formed in all monoxides; its relative abundance, in **5**, **6**, **9** and **10a–d**, is in the range of 50–80%).

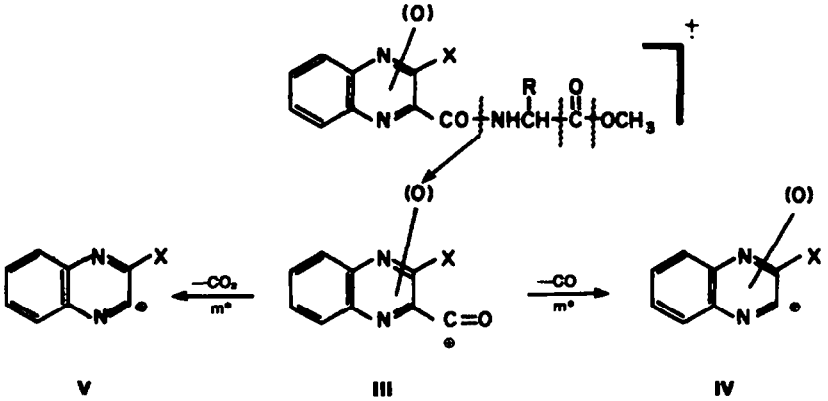
It has been noted earlier[2] that the amide bond in dioxides **7a–d** does not suffer cleavage to any appreciable extent before loss of *one* of the N-oxide oxygens (and hence to the abundance of ion III). The fact that the N-oxygenated quinoxalinium ion IV is also prominent in the MS of dioxides **7a–d** and **8a–d** suggests that the N-1-oxygen is selectively removed first under electron impact. In the amide monoxides **5**, **6**, **8** and **10a–d**, the M-16 peak is either not observed or is of low intensity (≤2%).

EXPERIMENTAL

M.ps were determined on Büchi SMP-20 apparatus and are uncorrected. NMR spectra were recorded on a Bruker WH-90 spectrometer equipped with Fourier transform facilities (^1H, 90 MHz; ^{13}C, 22.63 MHz) in $CDCl_3$ (for the esters) or in DMSO-d_6 (for the acids) with TMS as the internal reference. Optical rotations were taken on a Perkin–Elmer 241 polarimeter in $CHCl_3$ (*c*, 1–2) for the esters, and in DMF (*c*, 1–2) for the acids at 20°. Chemicals and other instruments (for UV, MS and preparative tlc), used in this study, have been described previously.[2,3] Elemental analysis were carried out at the laboratory of Dr. F. Pascher (Bonn).

N-(2-*Quinoxaloyl*)L-α-*amino ester*-1,4-*dioxides* (**8a–d**)

These compds were prepared via the interaction between **14b**[4] and the appropriate amino ester hydrochloride in DMF, in the presence of DPPA as the coupling reagent. The procedure is essentially analogous to that previously reported for related systems.[3,4] Yields were in the range of 50–65%. Analytical samples of the title compds were obtained using tlc plates; m.p. (°); $[\alpha]_D$ and (analysis) are given: **8a**: 158; +37.4° (Found: C, 52.2; H, 4.7; N, 13.0. Calc. for $C_{13}H_{13}N_3O_5$: C, 52.3; H, 4.7; N, 13.1%). **8b**: 108; +34.0° (Found: C, 56.6; H, 5.3; N, 13.2. Calc. for $C_{15}H_{17}N_3O_5$: C, 56.4; H, 5.4; N, 13.2%). **8c**: 172; +49.2° (Found: C, 61.0; H, 4.4; N, 11.8. Calc. for $C_{18}H_{15}N_3O_5$: C, 61.2; H, 4.3; N,



Scheme 2.

11.9%). **8d**: 152; +18.6° (Found: C, 62.2; H, 4.6; N, 11.3. Calc. for $C_{19}H_{17}N_3O_5$: C, 62.2; H, 4.7; N, 11.4%).

N-(2-*Quinoxaloyl*) L-α-*amino acid*-1,4-*dioxides* (**4a–d**)

The corresponding derivative **8a–d**, (0.01 mole) was dissolved in ethanolic NaOH (2%, 25 ml). The resulting soln was diluted immediately (1–2 min) with cold water (50 ml), filtered and the filtrate was acidified to pH 2 with 5N HCl. The title compds, precipitated as yellow solids in almost quantitative yields, were crystallized form MeOH, m.p (°); $[\alpha]_D$ and (analysis) are given: **4a**: 228 dec; +28.6° (Found: C, 51.8; H, 4.1; N, 15.0. Calc. for $C_{12}H_{11}N_3O_5$: C, 52.0; H, 4.0; N, 15.2%). **4b**: 216 dec; +35.1° (Found: C, 55.0; H, 5.0; N, 13.7. Calc. for $C_{14}H_{15}N_3O_5$: C, 55.1; H, 5.0; N, 13.8%). **4c**: 225 dec; +67.5° (Found: C, 60.2; H, 3.8; N, 12.2. Calc. for $C_{17}H_{13}N_3O_5$: C, 60.2; H, 3.9; N, 12.4%). **4d**: 197 dec; +29.6° (Found: C, 60.9; H, 4.2; N, 11.8. Calc. for $C_{18}H_{15}N_3O_5$: C, 61.2; H, 4.3; N, 11.9%).

3-*Methylquinoxaline*-2-*carboxylic acid*-1,4-*dioxide* (**13a**)

A suspension of **13b** (0.05 mole)[5] was heated (water bath, 80°), with shaking, until a clear yellow-orange soln was obtained (2–3 min). This alkaline soln was then cooled immediately, filtered, and the filtrate was acidified with 5N HCl to pH 2–3. The title acid, formed as yellow ppt in quantitative yield, was filtered and crystallized from MeOH, m.p. 168° dec. (Found: C, 54.2; H, 3.6; N, 12.8. Calc. for $C_{10}H_8N_2O_4$: C, 54.6; H, 3.7; N, 12.7%); ^{1}H NMR (δ): 2.47 (s, CH_3), 7.97 (m, H_6 and H_7), 8.44 (m, H_5 and H_8), 10.22 ppm (s, broad, CO_2H).

3-*Methylquinoxaline*-2-*carboxylic acid*-1-*oxide* (**15a**)

This acid was obtained in 85% yield by saponification (1N NaOH) of **15b**[5] in an analogous way to that described for the isomeric **11b**→**11a**,[5] m.p. 138°. (Found: C, 58.5; H, 3.9; N, 13.5. Calc. for $C_{10}H_8N_2O_3$: C, 58.8; H, 3.9; N, 13.7%); ^{1}H NMR (δ): 2.56 (s, CH_3), 7.86 (m, H_6 and H_7), 8.15 (m, H_5), 8.41 (m, H_8), 10.93 ppm (s, broad, CO_2H).

Quinoxaline-2-*carboxylic acid*-1-*oxide* (**16a**)

A soln of **17** (0.015 mole)[5] in glacial AcOH (50 ml) and H_2O_2 (30%, 15 ml) was set aside at room temp. The title monoxide, which separated slowly, was collected after 24 hr; m.p. 170° dec (lit.[4] 180–181). A later crop (collected after 72 hr) was shown, by ^{1}H NMR, to be a mixture of **16a** (40%; C_3–H, s, 9.48 ppm) and **14a** (60%; C_3–H, s, 8.34 ppm).

N-(3-*Methyl*-2-*quinoxaloyl*) L-*valine*-1,4-*dioxide* (**3b**) *and its methyl ester* **7b**

They were synthesized according to lit. procedures,[2] and were crystallized from MeOH, yield; m.p (°); $[\alpha]_{578}$ and (analysis) are now given: **3b**: 66%; 202 dec; +72.7° (Found: C, 56.2; H, 5.4; N, 13.0. Calc. for $C_{15}H_{17}N_3O_5$: C, 56.4; H, 5.4; N, 13.2%). **7b**: 58%; 152; +37.0° (Found: C, 57.4; H, 5.7; N, 12.6. Calc. for $C_{16}H_{19}N_3O_5$: C, 57.7; H, 5.8; N, 12.6%).

N-(2-*Quinoxaloyl*) L-α-*amino ester monoxides* (**6a–d** *and* **10a–d**) *and their* C_3-*methyl analogues* (**5a–d** *and* **9a–d**). *General procedures*

(i) *Sodium dithionite*.[4] This reagent (0.011 mole) was added in portions, during 2 min, to the particular amino acid -1,4-dioxide derivative (**3a–d** and **4a–d**, 0.01 mole) in NaOH aq (1N, 100 ml) at ambient temp. The mixture was stirred for additional 8–10 min, and filtered. The filtrate was acidified with 5N HCl and the ppt collected, dried, and esterified with diazomethane etherate. The resulting **5a–d** and **6a–d** were purified on tlc plates, yields were in the range of 45–60%.

Under identical conditions, **14a** gave the corresponding **12a** m.p. 182° dec (lit.[4] 180–182); ^{1}H NMR: 8.40 ppm (s, C_3–H). Similarly, the analogue **13a** gave **11a** m.p. 156 dec (lit.[3] 150–151).

(ii) *Trimethyl phosphite*.[5] A mixture of the quinoxaline amino ester-1,4-dioxide in question (0.01 mole) and trimethyl phosphite (Merck, 0.012 mole) in n-propanol (50 ml) was refluxed for 2.5 hr. The resulting clear soln was cooled and the precipitated monoxide was crystallized from MeOH, EtOH or $CHCl_3$–light-petroleum. In this way, **7a–d** gave **5a–d**, whereas **8a–d** (lacking the C_3-Me group) yielded **10a–d**. It is observed that **7c** and **8c** required excess phosphite (two fold) and longer reaction time (5 hr) for their clean monodeoxygenation. Yields were in the range of 70–80%.

Under these conditions, **14b**, gave however, a mixture of **16b** (10%) and **12b** (30%) together with unchanged starting **14d** (60%). No di-deoxygenated product was detected by ^{1}H NMR (absence of the C_3–H proton signal at 9.55 ppm).

Compound **15b** above, and **9a** (obtained via (iii) below) were also subjected to the action of trimethyl phosphite following the conditions noted above for the corresponding dioxides. No reduction products were detected; the monoxides were recovered unchanged. The oxides **6a** and **6c** lacking C_3-Me group (obtained via (i) above or (iii) below) were treated similarly, and were also recovered unchanged without loss in their optical activity.

(iii) *Coupling*. The reaction between **11a**, **12a**, **15a** and **16a** and the appropriate L-α-amino ester hydrochloride was carried out in DMF in the presence of DPPA following literature conditions.[3,6] The resulting **5,6,9** and **10a–d** were purified (tlc). Yields were in the range of 20–40%. Their identity with those obtained by procedures (i) and (ii) has been established by m.p and mixed m.p determinations and, where appropriate, comparison of their ^{1}H NMR and mass spectra and their behaviour on tlc.

(iv) *Peracid* N-*oxidation*. **2c** (0.01 mole) was dissolved in a mixture of AcOH (80 ml) and H_2O_2 (30%, 25 ml). The resulting mixture was heated at 50° for 24 hr, and then diluted with water (300 ml). The **6a** separated slowly as light-yellow stars upon standing at room temp. for 36 hr, and was purified on tlc plates (yield, 38%). The N-4-oxide assignment of the product follows from its identity in every respect with **6a** prepared via (i) or (iii) above. M.p (°); $[\alpha]_D$ and (analysis) for the monoxide isomerides are given: **5a**: 145; +53.0° (Found: C, 57.7; H, 5.2; N, 14.4. Calc. for $C_{14}H_{15}N_3O_4$: C, 58.1; H, 5.2; N, 14.5%). **9a**: 153; +65.5° (Found: C, 57.8; H, 5.2; N, 14.4%). **5b**: 96; +47.1° (Found: C, 60.6; H, 6.0; N, 13.2. Calc. for $C_{16}H_{19}N_3O_4$: C, 60.6; H, 6.0; N, 13.2%). **9b**: 140; +75.6° (Found: C, 60.5; H, 6.0; N, 13.2%). **5c**: 142; +14.5°. (Found: C, 64.8; H, 4.8; N, 11.8. Calc. for $C_{18}H_{17}N_3O_4$: C, 65.0; H, 4.9; N, 12.0%). **9c**: 150; +8.0° (Found: C, 64.5; H, 4.9; N, 11.9%). **5d**: 167; +35.6° (Found: C, 65.5; H, 5.2; N, 11.5. Calc. for $C_{20}H_{19}N_3O_4$: C, 65.7; H, 5.2; N, 11.5%). **9d**: 165; +11.2° (Found: C, 65.5; H, 5.3; N, 11.5%).

Compound **6a**: 130; +55.2° (Found: C, 56.5; H, 4.7; N, 15.1. Calc. for $C_{13}H_{13}N_3O_4$: C, 56.7; H, 4.8; N, 15.3%). **10a**: 126; +53.6° (Found: 56.8; H, 4.8; N, 15.2%). **6b**: 74; +49.8° (Found: C, 59.5; H, 5.7; N, 13.6. Calc. for $C_{15}H_{17}N_3O_4$: C, 59.4; H, 5.7; N, 13.9%). **10b**: 96; +51.6° (Found: C, 59.6; H, 5.6; N, 13.8%). **6c**: 133; +30.4°. (Found: C, 63.7; H, 4.4; N, 12.2. Calc. for $C_{18}H_{15}N_3O_4$: C, 64.1; H, 4.5; N, 12.5%). **10c**: 107; −24.2° (Found: C, 63.7; H, 4.4; N, 12.3%). **6d**: 72; +17.6° (Found: C, 64.7; H, 5.0; N, 11.9. Calc. for $C_{19}H_{17}N_3O_4$: C, 65.0; H, 4.9; N, 12.0%). **10d**: 132; −19.1° (Found: C, 64.9; H, 4.9; N, 11.9%).

Methyl quinoxaline-2-*carboxylate*-1-*oxide* **16b** *and the isomeric* **12b**

These compds were obtained by reacting **16a** and **12a** with CH_2N_2 etherate, m.p. (°); ^{1}H NMR (δ); and (analysis) are given: **16b**: 106; 9.08 (s, C_3–H), 8.59 (m, H_8), 8.15 (m, H_5), 7.82 (m, H_6 and H_7), 4.07 ppm (s, CO_2CH_3); (Found: C, 58.7; H, 3.9; N, 13.5. Calc. for $C_{10}H_8N_2O_3$: C, 58.8; H, 3.9; N, 13.7%). **12b**: 156; 9.03 (s, C_3–H), 8.57 (m, H_5), 8.17 (m, H_8), 7.89 (m, H_6 and H_7), 4.11 ppm (s, CO_2CH_3); (Found: C, 58.6; H, 3.8; N, 13.6%).

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