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# ASPECTS OF NITRILE OXIDE CYCLOADDITION STEREOSELECTIVITY: CHEMISTRY OF 4-CYANO-2,2-DIMETHYL- AND 4-CYANO-2,2,5,5-TETRAMETHYL-1,3-DIOXOLANE OXIDES. X-RAY STRUCTURE OF (4 RS, 5 RS)-4,5-BISMETHOXYCARBONYL-3-[(4 RS)-2,2,5,5-TETRAMETHYL-1,3-DIOXOLAN-4-YL]-$\Delta^2$-ISOXAZOLINE.

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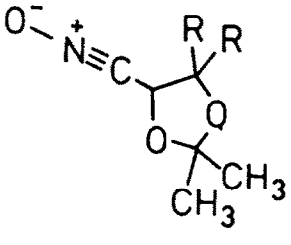
Abstract - 4-Cyano-2,2-dimethyl- and 4-cyano-2,2,5,5-tetramethyl-1,3-dioxolane oxides (1) and (2) were generated from the corresponding chloro-oximes, and trapped by addition to styrene, dimethyl maleate, dimethyl fumarate, and cyclopentene. The additions to styrene and dimethyl fumarate gave 1 : 1 mixtures of diastereoisomeric adducts. However some stereoselectivity was detected in the additions to the cis-1,2-disubstituted alkenes. The structure of (4 RS, 5 RS)-4,5-bismethoxycarbonyl-3-[(4 RS)-2,2,5,5-tetramethyldioxolan-4-yl]-$\Delta^2$-isoxazoline (17) was established by an X-ray structure determination.

$\Delta^2$-Isoxazolines, prepared by the cycloaddition of a nitrile oxide to an alkene, are now widely used in synthesis.[1] Whereas the addition of an achiral nitrile oxide to a chiral alkene has been shown, in some cases, to proceed with good diastereoselectivity,[2] the converse, i.e. the addition of a chiral nitrile oxide to an achiral alkene, has not been widely studied. We here report the generation and trapping of 4-cyano-2,2-dimethyl-, and 4-cyano-2,2,5,5-tetramethyl-1,3-dioxolane oxides (1) and (2).



(1) R = H

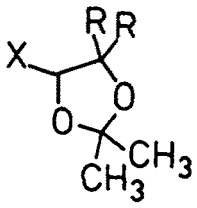
(2) R = $CH_3$

## RESULTS AND DISCUSSION

Nitrile oxides are usually generated *in situ* by dehydration of the corresponding nitro compound,[3] or by dehydrochlorination of a chloro-aldoxime.[4] In our hands attempts to prepare the 4-nitromethyl-dioxolane (4) by nitrite displacement of iodide from the 4-iodomethyl compound (3)[5] were thwarted by preferential formation of the nitrite ester (5), and so the chloro-aldoxime procedure was tried. Chloro-aldoxime (6) was prepared from the corresponding oxime by treatment with chlorine gas.[6] This gave one geometrical isomer (n.m.r.) of the chloroxime which was used without further purification.

Nitrile oxide (1) was generated by treatment of chloroxime (6) with triethylamine and trapped *in situ* by a series of alkenes. The results obtained are given in the Table. Since there was the possibility that a more hindered chiral nitrile oxide would show enhanced diastereoselectivity, the tetramethyl analogue (2) was generated from chloroxime (9), and trapped using alkenes. Chloroxime (9) was prepared from alcohol (7) *via* aldehyde (8).[7]

The results obtained using nitrile oxide (2) are also given in the Table.



(3) R = H, X = $ICH_2$-
(4) " X = $O_2NCH_2$-
(5) " X = O=NOCH$_2$-
(6) " X = HON=C(Cl)-
(7) R = $CH_3$, X = $CH_2OH$
(8) " X = CHO
(9) " X = HON=C(Cl)-

Table. Yields of Nitrile Oxide Adducts.

| Nitrile Oxide | Alkene | Cycloadducts % Yield[a] | Ratio[b] |
|---|---|---|---|
| (1) | styrene | 52 | 50 : 50 |
| " | di-Me fumarate | 62 | 50 : 50 |
| " | di-Me maleate | 33 | 70 : 30 |
| " | cyclopentene | 49 | 65 : 35 |
| (2) | styrene | 49 | 50 : 50 |
| " | di-Me fumarate | 61 | 50 : 50 |
| " | di-Me maleate | 36 | 75 : 25[c] |
| " | cyclopentene | 30 | 70 : 30 |

[a] Yields, not optimized, of purified products not allowing for nitrile oxide dimer. [b] Estimated by $^1$H n.m.r. integration of peaks in the spectrum of the crude product mixture. [c] Stereochemistry assigned : see text.

The nitrile oxides (1) and (2) were found to add to styrene and dimethyl fumarate to give 50 : 50 mixtures of isoxazolines (10) - (17) (see Scheme). However some diastereoselectivity was observed in the additions to the 1,2-cis-disubstituted alkenes, dimethyl maleate and cyclopentene. From the dimethyl maleate reactions, the two products isolated in each case were found to be identical to those isolated from the dimethyl fumarate reactions. It would appear that under the basic reaction conditions, epimerization of the cis-4,5-disubstituted isoxazolines (18) - (21) occurs at C(4). In addition to the isoxazoline products, the furoxan (26) was isolated from reactions of nitrile oxide (1). A minor product was detected in crude mixtures from reactions of nitrile oxide (2). It may have been furoxan (27) but was not isolated pure.

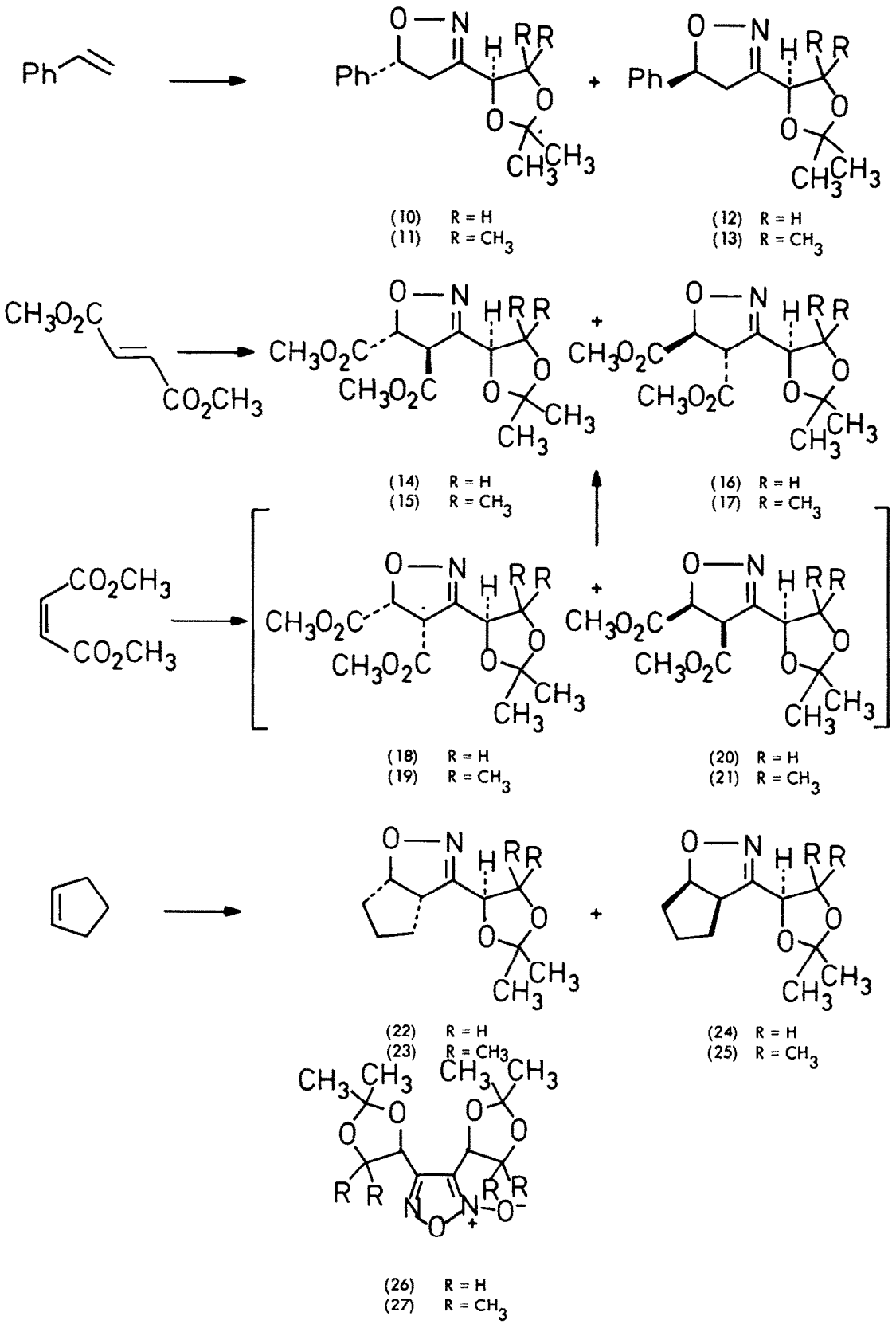
Structures were assigned to isoxazolines (10) - (25) on the basis of their spectroscopic data. These data did not allow stereochemical assignments to be made for each pair of diastereoisomeric products. Since the minor product from the dimethyl fumarate-tetramethyldioxolane nitrile oxide (2) was highly crystalline its structure was shown to be that depicted in formula (17) by a single crystal X-ray structure determination. The Figure shows a projection of the molecule which clearly demonstrates the relative configurations of the three chiral centres and which illustrates the crystallographic numbering scheme used. By analogy with the stereoselectivity in this reaction, the major product from the reaction between nitrile oxide (1) and dimethyl maleate was identified as isomer (14), after epimerization at C(4), and the major products in the cyclopentene reactions were identified as (22) and (23). Stereochemical assignments were not made for the styrene adducts (10) - (13).

It would appear that for the cases studied here, the chiral nitrile oxides (1) and (2) show only modest diastereoselectivity, and this is limited to cis-1,2-disubstituted alkenes. Perhaps this low diastereoselectivity is due to the exothermic nature of these cycloaddition reactions, since this implies an early transition state in which the two reagents are still somewhat separated, and in which steric interactions between the reagents are only weakly developed. It may be that the diastereoselectivity can be improved by introducing larger substituents into the dioxolane ring. However even the low diastereoselectivities observed here may be useful in reinforcing the intrinsic diastereoselectivity of a chiral alkene.

## EXPERIMENTAL

Melting points were measured on a Buchi 510 apparatus, and are uncorrected. I.r. spectra were measured on Perkin Elmer 257 and 297 spectrophotometers, and $^1$H n.m.r. spectra on a Bruker WH-300

SCHEME


Ph
(10) R = H
(11) R = CH3
(12) R = H
(13) R = CH3
CH3O2C
CO2CH3
(14) R = H
(15) R = CH3
(16) R = H
(17) R = CH3
(18) R = H
(19) R = CH3
(20) R = H
(21) R = CH3
(22) R = H
(23) R = CH3
(24) R = H
(25) R = CH3
(26) R = H
(27) R = CH3

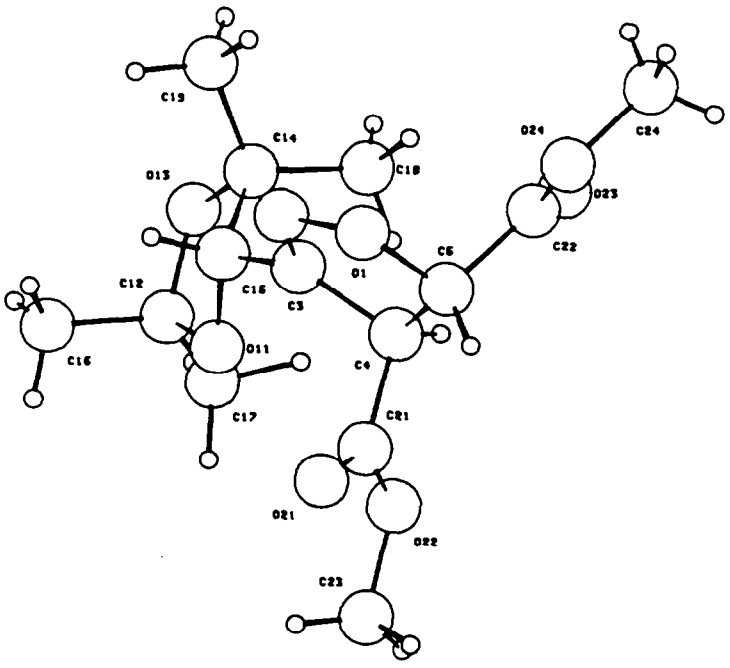



Figure: Ball and stick picture of isoxazoline (17) showing the crystallographic numbering scheme used. Drawn using SNOOPI (E.K. Davies, SNOOPI User Guide, Chemical Crystallography Laboratory, University of Oxford, Oxford, 1982).

spectrometer (300 MHz). Mass spectra were measured on a VG-micromass ZAB-16F spectrometer using the electron impact ionization mode.

Thin layer chromatography was carried out on Merck aluminium sheets, precoated with silica gel $60F_{254}$; flash chromatography was on Merck silica gel 60, and short column chromatography used Merck Keiselgel 60 H.

All solvents were dried and distilled before use. Ether refers to diethyl ether throughout, and light petroleum to the fraction boiling between 40 and 60°C.

2,2-Dimethyl-4-formyl-1,3-dioxolane Chloro-oxime (6). 2,2-Dimethyl-4-formyl-1,3-dioxolane (0.985g, 7.57 mmol) in ethanol (5 ml) was added at O°C to a solution of NaOH (0.62g, 15.5 mmol) and $NH_2OH.HCl$ (1.08g, 15.5 mmol) in ethanol (30 ml). After 30 min at O°C, the mixture was heated under reflux for 10 min, cooled, filtered, and concentrated under reduced pressure. Extraction into ether gave a mixture of syn- and anti-oximes (5) (0.91g, 80%). $^1H$ NMR ($CDCl_3$) δ 1.40 and 1.46 (each 3 H, s, $CH_3$), 3.78 (1/3 H,dd, J 7.5, 9 Hz, HCHO of syn-isomer), 3.86 (2/3 H,dd, J 6.5, 9 Hz, HCHO of anti-isomer), 4.17 (2/3 H,dd, J 9, 9.5 Hz, HCHO of anti-isomer), 4.36 (1/3 H,dd, J 7, 9 Hz, HCHO of syn-isomer), 4.64 (2/3 H, q, J 7 Hz, CHO of anti-isomer), 5.11 (1/3 H,dt, J 4, 7 Hz, CHO of syn-isomer), 6.95 (1/3 H,d, J 4 Hz, CHN of syn-isomer), 7.39 (2/3 H,d, J 7 Hz, CHN of anti-isomer), and 8.8 (1 H, br. s, OH).

Dry chlorine gas was bubbled through a stirred solution of oximes (5) (0.34g, 2.3 mmol) in anhydrous ether (60 ml) at -60°C for 25 min. After warming to 20°C, the ether was removed under reduced pressure, and the impure chloro-oxime dissolved in benzene. Removal of the benzene under reduced pressure gave 4-formyl-2,2-dimethyl-1,3-dioxolane chloro-oxime (6) (0.38g, 92%) as a white solid, used without further purification. IR ($CHCl_3$) $\nu_{max.}$ 3 560, 3 320, 1 630, 1 150, 1 070, 975, 930, and 845 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.44 and 1.55 (each 3 H, s, $CH_3$), 4.23 (2 H, m, $CH_2O$), 4.83 (1 H, t, J 6.3 Hz, CHO), and 8.12 (1 H, s, OH); MS m/z 164, 166 ($M^+$ - 15).

4-Formyl-2,2,5,5-tetramethyl-1,3-dioxolane (8). DMSO (1.06 ml, 13.7 mmol) in $CH_2Cl_2$ (3.2 ml) was added to oxalyl chloride (0.62 ml, 6.88 mmol) in $CH_2Cl_2$ (16 ml) under nitrogen at -55°C. A solution of 4-hydroxymethyl-2,2,5,5-tetramethyl-

1,3-dioxolane (7) (1.01g, 6.33 mmol) in $CH_2Cl_2$ (7 ml) was added dropwise. After 5 min, $Et_3N$ (4.4 ml) was added dropwise, and after a further 5 min the mixture was allowed to warm to 20°C. After washing with water and brine, concentration under reduced pressure gave an oil, which was distilled to give 4-formyl-2,2,5,5-tetramethyl-1,3-dioxolane (8) (0.485 g, 49%), as a colourless oil, b.p. 85°C/2 mm. Hg. IR (film) $\nu_{max.}$ 3 450, 1 735, 1 370, 1 220, 1 195, 1 130 1 070, 1 000; 915, and 855 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.19, 1.38, 1.41, and 1.51 (each 3 H, s, $CH_3$), 4.08 (1 H, d, J 1.3 Hz, CH CHO), and 9.65 (1H, d, J 1.3 Hz, CH CHO); MS m/z 143 ($M^+$ -15) and 129 ($M^+$ -29).

4-Formyl-2,2,5,5-tetramethyl-1,3-dioxolane Chloro-oxime (9). Aldehyde (8) was converted into a mixture of syn- and anti-oximes using the procedure described above (86%). IR (film) $\nu_{max.}$ 3 350, 1 370, 1 260, 1 220, 1 195, 1 060, 1 000, 945, and 860 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.22, 1.34, 1.42, and 1.51 (each 3 H, s, $CH_3$), 4.32 (2/3 H, d, J 7 Hz, CHO of anti-isomer), 5.06 (1/3 H, d, J 6 Hz, CHO of syn-isomer), 6.83 (1/3 H, d, J 6 Hz, CHN of syn-isomer), 7.41 (2/3 H, d, J 7 Hz, CHN of anti-isomer), and 8.3 (1 H, br. s, OH); MS m/z 158 ($M^+$ -15).

A mixture of these oximes (0.43 g, 2.48 mmol) was treated with chlorine gas as described above to give 4-formyl-2,2,5,5-tetramethyl-1,3-dioxolane chloro-oxime (9) (0.5 g, 98%) as a pale green waxy solid used without further purification. IR ($CHCl_3$) $\nu_{max.}$ 3 560, 3 320, 1 380, 1 260, 1 220, 1 195, 1 130, 1 060, 1 000, and 860 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.22, 1.41, 1.48, and 1.53 (each 3 H, s, $CH_3$), 4.52 (1 H, s, CHO), and 8.8 (1 H, br. s, OH); MS m/z 192, 194 ($M^+$ -15).

General Procedure for $\Delta^2$-Isoxazoline Preparation. A solution of triethylamine (1.5 molar equivs.) in ether was added dropwise to a solution of chloro-oxime (1 molar equiv.) and the alkene (1.2 molar equivs.) in ether at 0°C. The mixture was then stirred for 14-20h at 20°C, diluted with $CHCl_3$, washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The crude products so obtained were found to contain the desired $\Delta^2$-isoxazolines together with, in some cases, unchanged alkene and nitrile oxide dimer. No attempts were made to optimize yields. Flash, or short column chromatography, gave pure products for characterization.

3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-phenyl-$\Delta^2$-isoxazolines (10) and (12). Styrene (0.225 g, 2.16 mmol), chloro-oxime (6) (0.373 g, 2.08 mmol), and triethylamine (0.434 ml, 3.12 mmol), after 18h at 20°C, gave a crude product mixture shown, by $^1H$ n.m.r., to contain $\Delta^2$-isoxazolines (10) and (12), furoxan (26), and unchanged styrene, mole ratio 30:30:25:15, respectively. Flash chromatography (light petroleum-ether, 2:1) gave $\Delta^2$-isoxazolines (10) and (12), together with furoxan (26) (0.266g, 52%). The faster moving 3-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-phenyl-$\Delta^2$-isoxazoline, $R_f$ 0.26, was an oil, inseparable from a small amount (10%) of furoxan (26). IR (film) $\nu_{max.}$ 1 250, 1 215, 1 150, 1 060, 840, 760, and 700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.40 and 1.43 (each 3 H, s, $CH_3$), 3.02 (1 H, dd, J 8.8, 17.5 Hz, HCHCN), 3.83 (1 H, dd, J 11.5, 17.5 Hz, HCHCN), 3.98 (1 H, dd, J 6.5, 8.5 Hz, HCHO), 4.24 (1 H, dd, J 6.5, 8 Hz, HCHO), 5.02 (1 H, t, J 6Hz, CHO), 5.65 (1 H, dd, J 8.8, 11.5 Hz, PhCHO), and 7.35 (5 H, m, aromatic H); MS m/z 247 ($M^+$), 232 ($M^+$ - 15), and 190 ($M^+$ - 57) (Found: $M^+$ 247.1209. $C_{14}H_{17}NO_3$ requires M, 247.1208). The slower moving 3-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-phenyl-$\Delta^2$-isoxazoline, $R_f$ 0.18, was a crystalline solid, m.p. 88°C (from ether-light petroleum). IR ($CHCl_3$) $\nu_{max.}$ 1 630, 1 260, 1 210, 1 150, 1 060, and 840 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.43 and 1.46 (each 3 H, s, $CH_3$), 3.10 (1 H, dd, J 10, 17.5 Hz, HCHCN), 3.38 (1 H, dd, J 11.3, 17.5 Hz, HCHCN), 4.08 (1 H, dd, J 6.5, 8.8 Hz, HCHO), 4.29 (1 H, dd, J 6.5, 8.8 Hz, HCHO), 5.0 (1 H, t, J 7 Hz, CHO), 5.63 (1 H, dd, J 10, 11.3 Hz, PhCHO), and 7.35 (5 H, m, aromatic H); MS m/z 247 ($M^+$), 232 ($M^+$ -15), and 190 ($M^+$ -57) (Found: C, 68.1; H, 7.0; N, 5.7. $C_{14}H_{17}NO_3$ requires C, 68.0; H, 6.9; N, 5.7%).

5-Phenyl-3-(2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)-$\Delta^2$-isoxazolines (11) and (13). Styrene (0.115g, 1.10 mmol), chloro-oxime (9) (0.187g, 0.9 mmol), and triethylamine (0.88 ml, 1.35 mmol) after 14h at 20°C gave a crude product mixture shown by $^1$H n.m.r. to contain $\Delta^2$-isoxazolines (11) and (13), unchanged styrene, and furoxan (27) (tentative assignment, $^1$H n.m.r. δ5.04, 5.05), mole ratio 35:35:25:5, respectively. Flash chromatography (light petroleum-ether, 2:1) gave an inseparable mixture of 5-phenyl-3-(2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)-$\Delta^2$-isoxazolines (11) and (13) (0.12g, 49%) as a colourless oil. IR (film) $\nu_{max.}$ 1 605, 1 320, 1 220, 1 195, 1 125, 1 070, 1 000, 860, and 700 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ1.06, 1.24, 1.40, 1.41, 1.43, 1.45, 1.49, and 1.50 (each 3 H, s, $CH_3$), 3.06 and 3.17 (each 1 H, dd, J 8.8, 17.5 Hz, HCHCN), 3.49 and 3.59 (each 1 H, dd, J 11.3, 17.5 Hz, HCHCN), 4.69 (2 H, s, CHO of both isomers), 5.63 (2 H, m, PhCHO of both isomers), and 7.35 (10 H, m, aromatic H of both isomers); MS m/z 260 ($M^+$ -15), 217 ($M^+$ - 58), and 111 ($M^+$ - 164).

(4 RS, 5 RS)-4,5-Bismethoxycarbonyl-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-$\Delta^2$-isoxazolines (14) and (16). Dimethyl fumarate (0.367g, 2.54 mmol), chloro-oxime (6) (0.455g, 2.54 mmol), and triethylamine (0.53 ml, 3.81 mmol) gave, after 16h at 20°C, a crude product mixture containing $\Delta^2$-isoxazolines (14) and (16), ratio 50:50, as major components, together with traces of furoxan (26) and unchanged dimethyl fumarate. Short column chromatography (light petroleum-ether, 1:1) gave (4 RS, 5 RS)-4,5-bismethoxycarbonyl-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-$\Delta^2$-isoxazolines (14) and (16) (62%), an inseparable mixture, as an oil. IR (film) $\nu_{max.}$ 1 740 1 370, 1 220, 1 060, 1 015, 890, 840, and 730 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ1.38, 1.41, 1.43, and 1.46 (each 3 H, s, $CH_3$), 3.79 (3 H, s, $OCH_3$), 3.80 (6 H, s, 2 x $OCH_3$), 3.83 (3 H, s, $OCH_3$), 4.2 (4 H, m, $CH_2O$ of both isomers), 4.47 (1 H, d, J 7.5 Hz, CHCN), 4.56 (1 H, d, J 6 Hz, CHCN), 4.95 and 5.06 (each 1 H, t, J 6 Hz, CNCHO of each isomer), 5.30 (1 H, d, J 7.5 Hz, CHO), and 5.34 (1 H, d, J 6 Hz, CHO); MS m/z 272 ($M^+$ - 15) (Found: $M^+$ - $CH_3$, 272.0770. $C_{11}H_{14}NO_7$ requires M, 272.0770).

Dimethyl maleate (0.233g, 1.54 mmol), chloro-oxime (6) (0.266g, 1.48 mmol), and triethylamine (0.31g, 2.22 mmol) after 16h at 20°C gave a crude product mixture shown by $^1$H n.m.r. to contain $\Delta^2$-isoxazolines (14) and (16) together with unchanged maleate and a substantial amount of furoxan (26), mole ratio 15:5:55:25, respectively. Flash chromatography (light petroleum-ether, 4:3) gave firstly the furoxan (26) (0.13g, 61%), as a colourless oil. IR (film) $\nu_{max.}$ 1 610, 1 382, 1 372, 1 220, 1 150, 1 070, and 845 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.43, 1.46, 1.48, and 1.53 (each 3 H, s, $CH_3$), 4.28 and 4.37 (each 2 H, m, $CH_2$), 5.22 (1 H, t, J 7.5 Hz, CHO), and 5.29 (1 H, dd, J 5.5, 6.5 Hz, CHO); MS m/z 271 ($M^+$ - 15). Secondly $\Delta^2$-isoxazolines (14) and (16) (0.14g, 33%) were eluted, and shown to be identical with authentic samples.

(4 SR, 5 SR)-4,5-Bismethoxycarbonyl-3-(2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)-$\Delta^2$-isoxazolines (15) and (17). Dimethyl fumarate (0.187g, 1.3 mmol), chloro-oxime (9) (0.285g, 1.37 mmol), and triethylamine (0.29 ml, 2.1 mmol) after 15h at 20°C gave the $\Delta^2$-isoxazolines (15) and (17), ratio 50:50, together with unchanged fumarate. Short column chromatography (light petroleum-ether, 1:1) separated the $\Delta^2$-isoxazolines. The first eluted isomer was identified as (4 SR, 5 SR)-4,5-bismethoxycarbonyl-3-[(4 SR)-2,2,5,5-tetramethyl-1,3-dioxolan-4-yl]-$\Delta^2$-isoxazoline (17) (26%), a white crystalline solid, m.p. 101°C (from ether-light petroleum). IR ($CHCl_3$) $\nu_{max.}$ 1 745, 1 220, 1 192, 1 125, 1 070, 1 000, and 855 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.20, 1.38, 1.44, and 1.47 (each 3 H, s, $CH_3$), 3.80 and 3.84 (each 3 H, s, $OCH_3$), 4.51 (1 H, d, J 6.3 Hz, CHCN), 4.75 (1 H, s, CHO), and 5.25 (1 H, d, J 6.3 Hz, CHO); MS m/z 300 ($M^+$ - 15) and 198 ($M^+$ - 117) (Found: C, 53.5; H, 6.9; N, 4.5. $C_{14}H_{21}NO_7$ requires C, 53.3; H, 6.7; N, 4.4%). The second eluted isomer was identified as (4 RS, 5 RS)-4,5-bismethoxycarbonyl-3-[(4 SR)-2,2,5,5-tetramethyl-1,3-dioxolan-4-yl]-$\Delta^2$-isoxazoline (15) (28%), a white crystalline solid, m.p. 66-67°C (from ether-light petroleum). IR ($CHCl_3$) $\nu_{max.}$ 1 745, 1 210, 1 125, 1 000, and 860 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ

1.18, 1.40, 1.48, and 1.50 (each 3 H, s, $CH_3$), 3.82 and 3.84 (each 3 H, s, $OCH_3$), 4.43 (1 H, d, J 6.3 Hz, CHCN), 4.70 (1 H, s, CHO), and 5.34 (1 H, d, J 6.3 Hz, CHO); MS m/z 300 ($M^+$ - 15) and 198 ($M^+$ - 117) (Found: C, 53.3; H, 6.60; N, 4.4%).

Dimethyl maleate (0.186g, 1.29 mmol ), chloro-oxime (9) (0.26g, 1.25 mmol ), and triethylamine (0.26 ml, 1.86 mmol), after 16h at 20°C, gave a crude product mixture containing unchanged maleate, $\Delta^2$-isoxazolines (15) and (17), and a trace of dimer (?), mole ratio 45:38:12:5, respectively. Short column chromatography separated the $\Delta^2$-isoxazolines (15) and (17) (combined yield 36%), shown to be identical with authentic samples.

4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-oxa-3-azabicyclo-[3.3.0]oct-3-enes (22) and (24). Chloro-oxime (6) (0.2g, 1.12 mmol) and triethylamine (0.32 ml, 2.3 mmol) in cyclopentene (25 ml) after 2h at 20°C gave a crude product containing the $\Delta^2$-isoxazolines (22) and (24), ratio 65:35, together with minor impurities. Flash chromatography (ether-light petroleum, 1:1) gave an inseparable mixture of 4-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxa-3-azabicyclo-[3.3.0]oct-3-enes (22) and (24) (49%), as a colourless oil. IR (film) $\nu_{max.}$ 1 615, 1 450, 1 380, 1 370, 1 210, 1 150, 1 060, 900, and 840 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.40 (6 H, s, 2 x $CH_3$), 1.44 and 1.47 (each 3 H, s, $CH_3$), 1.7 and 2.1 (each 6 H, m, 3 x $CH_2$ of both isomers), 3.70 (2 H, m, CHCN of both isomers), 4.1 and 4.2 (each 2 H, m, HCHO of both isomers), and 4.87 and 5.08 (each 2 H, m, CHO of both isomers); MS m/z 211 ($M^+$), 196 ($M^+$ - 151, and 154 ($M^+$ - 57) (Found: $M^+$ 211.1207. $C_{11}H_{17}NO_3$ requires M, 211.1208).

4-(2,2,5,5-Tetramethyl-1,3-dioxolan-4-yl)-2-oxa-3-azabicyclo-[3.3.0]oct-3-enes (23) and (25). Chloro-oxime (9) (0.16g, 0.75 mmol) and triethylamine (0.21g, 1.5 mmol) in cyclopentene (50 ml) after 2h at 20°C gave a complex mixture of products. Flash chromatography separated the desired $\Delta^2$-isoxazolines. The first eluted isoxazoline was identified as (1 SR, 5 SR)-4-[(4 SR)-2,2,5,5-tetramethyl-1,3-dioxolan-4-yl]-2-oxa-3-azabicyclo[3,3,0]oct-3-ene (23), a colourless oil. IR (film) $\nu_{max.}$ 1 370, 1 265, 1 195, 1 130, 1 070, 1 000, 915, and 860 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.20, 1.38, 1.40, and 1.50 (each 3 H, s, $CH_3$), 1.2-2.2 (6 H, m, 3 x $CH_2$), 3.73 (1 H, m, CHCN), 4.60 (1 H, s, CHO), and 5.08 (1 H, m, CHO); MS m/z 224 ($M^+$ - 15) and 181 ($M^+$ -58) (Found: $M^+$ - $CH_3$, 224.1287. $C_{12}H_{18}NO_3$ requires M, 224.1287). The second eluted isoxazoline was identified as (1 RS, 5 RS)-4-[(4 SR)-2,2,5,5-tetramethyl-1,3-dioxolan-4-yl]-2-oxa-3-azabicyclo[3.3.0]oct-3-ene (25), a colourless oil. IR (film) $\nu_{max.}$ 1 370, 1 195, 1 125, 1 000, 900, and 860 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.20, 1.42, 1.48, and 1.53 (each 3 H, s, $CH_3$), 1.2-2.2 (6 H, m, 3 x $CH_2$), 3.64 (1 H, m, CHCN), 4.53 (1 H, s, CHO), and 5.08 (1 H, m, CHO); MS m/z 224 ($M^+$ - 15).

X-Ray Structure Determination for $\Delta^2$-Isoxazoline (17). Crystal Data. $C_{14}H_{21}NO_7$, M = 315.3, orthorhombic, a = 7.642 (1), b = 16.812 (2), c = 24.822 (2) Å, U = 3075.3 $Å^3$, Z = 8, $D_c$ = 1.36g $cm^{-3}$, μ (Cu-Kα) = 9.4 $cm^{-1}$, space group Pbca.

A transparent crystal of $\Delta^2$-isoxazoline (17) was obtained from a 1:1 mixture of light petroleum and ether, which had approximate dimensions of 0.6 x 0.4 x 0.3 mm. Data collection was performed with a CAD-4 computer controlled diffractometer, equipped with a graphite crystal monochromator. Data were collected using the ω-2θ scan technique for reflections having $4^\circ \leqslant 2\theta \leqslant 150^\circ$. The scan rate varied between 6.7 and 1.5 °/min. A total of 2911 unique reflections were measured which were corrected for Lorentz and polarization effects, but not for absorption effects. The structure was solved using MULTAN 80[8] and refined with isotropic temperature factors by full matrix least squares using the 1860 reflections having $I \geqslant 3\sigma(I)$. The refinement was continued by blocked-matrix least squares using anisotropic temperature factors. All the hydrogen atoms were located by the difference Fourier technique, and included in the refinement (coordinates and isotropic temperature factors).

An extinction correction was applied during the

final stages of refinement, and the weight for each reflection was calculated from the Chebyshev series $W = [376{\cdot}5\ t_o(X) + 509.7\ t_1(X) + 138.9\ t_x(X)]^{-1}$ where $X = Fo/F_{max}$.

The refinement converged at a Final R value of 4.9%. All calculations were performed with the CRYSTALS[10] package on the Chemical Crystallography Laboratory VAX 11/750 computer.

Tables of bond distances and bond angles have been deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EN.

A table of the observed and calculated structure factors has been presented for deposition with the British Library, Lending Division.

The $\Delta^2$-isoxazoline and 1,3-dioxolane rings both have envelope conformations, with the 1,3-dioxolane ring being the more puckered. Bond lengths and angles are similar to those observed in other $\Delta^2$-isoxazolines, the C(4) - C(3) - C(15) angle enlargement being a common feature. The opening out of the C(3) - C(15) - C(14) angle to 116.7° is probably an attempt to relieve steric strain between C(15) and C(19) which have a separation of 3.37 Å.

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