Pyrazine Chemistry. Part 10.[1] Synthesis of Alkylated Derivatives of Piperazine-2,5-diones

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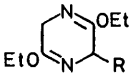
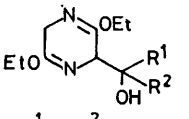
A general method is presented for the elaboration of 3-monosubstituted and 3,6-disubstituted piperazines and pyrazines. The method proceeds *via* prior formation of 2,5-diethoxy-3,6-dihydropyrazine, by reaction of the appropriate piperazine-2,5-dione with Meerwein's salt. These dihydropyrazines readily condense with either aldehydes or ketones and can be alkylated with alkyl or allyl bromides. Unsymmetrically substituted pyrazines can be prepared from the dihydro-intermediates by mild oxidation.

In recent years a wide range of dioxopiperazines have been identified as natural metabolites, many of which possess interesting biological properties.[2] As part of a general programme aimed at the synthesis of such systems, it became necessary to extend the carbon skeleton of simple members of the 2,5-dioxopiperazine group. Previous work in this area has been reported.[3] Condensation of aldehydes onto these ring systems can be effected, especially after protection of the amide functions by prior acetylation, but the method is limited in its application, since ketones are relatively inactive and sequential condensations, at both positions 3 and 6, can only be achieved if the first condensation is carried out with aryl carbonyl compounds.

Direct alkylation of 2,5-dioxopiperazine has not been reported in the literature. Our attempts to alkylate the parent compound, or 3-substituted members of this family, using a variety of conditions, always gave low yields of the desired products.



(1) R = H
(2) R = $CH_2CH{=}CH_2$
(3) R = $CH_2C(Me){=}CH_2$
(4) R = $[CH_2]_3O$—tetrahydropyran-2-yl



(5) R^1 = H, R^2 = Ph
(6) R^1 = H, R^2 = $C(Me){=}CH_2$
(7) R^1 = Me, R^2 = $CH{=}CH_2$
(8) R^1 = R^2 = Me

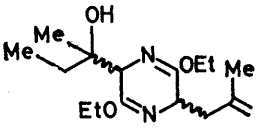
Recently the alkylation of imino-ethers at low temperatures in tetrahydrofuran using lithium bases has been reported.[4] Since bis-imino ethers (1) of 2,5-dioxopiperazines are readily prepared by the action of Meerwein salts,[5] the alkylation of these derivatives has been examined.

RESULTS AND DISCUSSION

Formation of the monoanion from the dihydropyrazine (1), using lithium di-isopropylamide followed by reaction with allyl bromide, afforded, after work-up, 3-allyl-2,5-diethoxy-3,6-dihydropyrazine (2) in 52% yield. In a similar manner, the 2-methylallyl derivative (3) was also formed. Alkylations could also be achieved with simple alkyl halides, such as 3-bromopropyl tetrahydropyran-2-yl ether, which afforded the mono-alkylated dihydropyrazine (4) in good yield.

The conditions employed for generating the imidate anion were also suitable in the condensations of aldehydes and ketones with the dihydropyrazine. In no case was dehydration to the alkylidenedihydropyrazine observed. Condensation with benzaldehyde gave the benzyl alcohol (5). Two diastereoisomeric alcohols may be expected from this condensation. From our reaction the product was obtained as a crystalline solid (51%), which behaved as a single isomer of unknown stereochemistry. With either methacrylaldehyde or methyl vinyl ketone the analogous condensates, (6) and (7) respectively, formed as oils. Again these appeared to consist of one major isomer (^1H n.m.r. analysis) and in neither case was conjugate addition observed. The generality of these condensation reactions was illustrated by use of acetone, which gave the expected product (8).

A second substituent could be introduced into the monosubstituted dihydropyrazines by repetition of the alkylation or condensation process. Thus 2,5-diethoxy-



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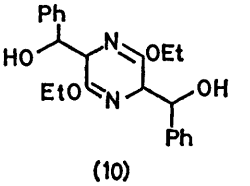

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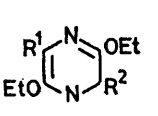
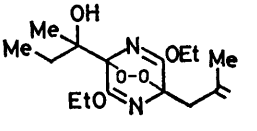


(11) R^1 = H, R^2 = $C(OH)Me_2$
(12) R^1 = H, R^2 = $C(Me){=}CH_2$
(13) R^1 = H, R^2 = CH(OH)Ph
(14) R^1 = H, R^2 = COPh
(15) R^1 = H, R^2 = $[CH_2]_3O$—tetrahydropyran-2-yl
(16) R^1 = H, R^2 = $[CH_2]_3OH$
(17) R^1 = H, R^2 = $CH_2C(Me){=}CH_2$
(18) R^1 = $CH_2C(Me){=}CH_2$, R^2 = C(Me)(OH)Et



(19)

3-(2-methylallyl)-3,6-dihydropyrazine (6) could be condensed with methyl ethyl ketone to give the adduct (9), as a mixture of isomers, bearing the carbon skeleton of bicyclomycin.[6] Similarly, condensation of a second

mole of benzaldehyde with the crystalline adduct (5) gave the disubstituted material (10), as a mixture of isomers.

The dihydropyrazines were readily dehydrogenated with dichlorodicyanobenzoquinone (DDQ) [5] to afford the corresponding pyrazines. The product of oxidation of the acetone adduct, (8), was the pyrazine (11) and this could be dehydrated, using toluene-*p*-sulphonic acid and molecular sieves in benzene, to give the isopropenyl-substituted pyrazine (12). With the benzyl alcohol (5), the major product of dehydrogenation was the corresponding pyrazine (13), accompanied by smaller quantities of the benzoyl-substituted pyrazine (14), thus indicating that ring dehydrogenation occurs in preference to allylic oxidation. For the propyl compound (4), oxidation afforded the substituted pyrazine (15). Subsequent hydrolytic removal of the tetrahydropyranyl ether group gave the corresponding alcohol (16) in high yield. Dehydrogenation of the 2-methylallyl derivative (3) proceeded with no complications owing to the allylic hydrogens and the required pyrazine (17) was readily obtained when one equivalent of DDQ was used.

As reported previously,[7] the pyrazines are subject to attack by singlet oxygen. After dehydrogenation of the mixture of isomers (9), the single pyrazine (18) so formed was reacted with singlet oxygen to give the *endo*-peroxide (19). Although the isolated double bond of the 2-methylallyl group would be expected to be itself susceptible to attack by singlet oxygen, to form an allylic hydroperoxide by an ene-type oxidation, this transformation was not observed under our reaction conditions, involving the addition of 1 mole of oxygen.

EXPERIMENTAL

For general experimental details see ref. 1. Light petroleum refers to the fraction of boiling range 40—60 °C.

General Procedure for Alkylations and Condensations.—To a cooled (−78 °C), stirred, solution of dry di-isopropylamine (1.1 equiv.) in dry THF, under oxygen-free N_2, was added butyl-lithium (1.1 equiv.). The solution was stirred for 30 min and a solution of the imino-ether (1 equiv.) in dry THF was then added and stirring continued at −78 °C for a further 90 min. The alkylating agent, aldehyde, or ketone (1 equiv.) was then injected into the solution, stirring continued at −78 °C for 3 h, and the mixture then allowed to warm to room temperature (4—21 h). The mixture was then poured into ether, washed with aqueous sodium chloride solution, dried, and concentrated.

3-*Allyl*-2,5-*diethoxy*-3,6-*dihydropyrazine* (2).—2,5-Diethoxy-3,6-dihydropyrazine (1) (DEDP) (0.2 g, 1.2 mmol) was metallated with lithium di-isopropylamide and alkylated with allyl bromide (0.14 ml, 1.2 mmol). After stirring the reaction mixture for 16 h it was worked up to give, after p.l.c. ($CHCl_3$), the *title compound* (2) as a pale yellow oil (52%); $\nu_{max.}$ (film) 2 970, 2 920, 1 690, 1 435, 1 365, 1 340, 1 135, 1 090, 1 030, and 910 cm^{-1}; τ 8.76 (6 H, t, *J* 6 Hz), 7.52 (2 H, t, *J* 6 Hz), 6.0 (7 H, m), and 5.1—4.16 (3 H, m); *m/e* 228 ($[M + H_2O]^+$, 25%), 227 (33), 210 (M^+, 8), 169 (100), 153 (25), 141 (58), 113 (58), 85 (100), 57 (42), and 55 (33) (Found: M^+, 228.146 8. $C_{11}H_{18}N_2O_2 \cdot H_2O$ requires *M*, 228.147 4).

2,5-*Diethoxy*-3-(2-*methylallyl*)-3,6-*dihydropyrazine* (3).—By the standard procedure, DEDP (3 mmol) was alkylated with 2-methylallyl bromide. After work-up and chromatography (Al_2O_3, grade III; 20 g), elution with light petroleum afforded the *product* as a colourless oil (70%); $\nu_{max.}$ (film) 3 000—2 800, 1 690, 1 440, 1 365, 1 340, 1 240, 1 140, 1 090, 1 030, and 890 cm^{-1}; τ 8.76 (6 H, t, *J* 6 Hz), 8.28 (3 H, br s), 7.62 (2 H, d, *J* 4 Hz), 6.12—5.92 (7 H, m), and 5.32 (2 H, d, *J* 4 Hz); *m/e* 224 (M^+, 42%), 222 (7), 170 (9), 169 (100), 141 (45), 113 (38), 85 (45), 56 (10), and 55 (9) (Found: M^+, 224.152 4. $C_{12}H_{20}N_2O_2$ requires *M*, 224.152 5).

2,5-*Diethoxy*-3-(3-*tetrahydropyran*-2-*yloxypropyl*)-3,6-*dihydropyrazine* (4).—DEDP (1.2 mmol) was alkylated with 1-tetrahydropyran-2-yloxy-3-bromopropane (0.3 g, 1.2 mmol). The product was isolated as an oil (67%) after column chromatography (Al_2O_3, grade III), eluting with $CHCl_3$; $\nu_{max.}$ 2 980—2 860, 1 690, 1 480—1 440, 1 370, 1 345, 1 240, 1 135, 1 120, 1 030, 900, 815, and 755 cm^{-1}; τ 8.80 (6 H, t, *J* 6 Hz), 8.6—7.7 (10 H, m), 6.7—6.2 (4 H, m), 6.1—5.8 (7 H, m), and 5.5 (1 H, br s); *m/e* 312 (M^+, 7%), 229 (9), 228 (77), 227 (100), 211 (31), 119 (27), 183 (45), 181 (20), 169 (47), 155 (10), 154 (11), 153 (39), and 85 (84) (Found: M^+, 312.2053. $C_{16}H_{28}N_2O_4$ requires *M*, 312.205 0).

2,5-*Diethoxy*-3-(α-*hydroxybenzyl*)-3,6-*dihydropyrazine* (5).—DEDP (1.2 mmol) was metallated with lithium di-isopropylamide before condensing with benzaldehyde (0.15 ml, 1.2 mmol). The principal aldol was isolated as colourless needles (51%), m.p. (light petroleum) 121—122 °C; $\nu_{max.}$ 3 420, 1 685, 1 370, 1 250, 1 130, 1 090, 1 080, 1 060, 1 030, 725, and 695 cm^{-1}; $\lambda_{max.}$ (EtOH) 208 nm (ε 8 585); τ 8.74 (6 H, t, *J* 3 Hz), 7.12—5.44 (8 H, m), 4.88 (1 H, br s, sharpened on D_2O exchange), and 2.85 (5 H, m) (Found: C, 65.6; H, 7.5; N, 10.1. $C_{15}H_{20}N_2O_3$ requires C, 65.2; H, 7.2; N, 10.1%).

2,5-*Diethoxy*-3-(2-*hydroxy*-2-*methylallyl*)-3,6-*dihydropyrazine* (6).—Using the procedure described above, DEDP (1.2 mmol) was condensed with freshly distilled methacrylaldehyde (0.1 ml, 1.2 mmol). The residue, after work-up, was chromatographed (Al_2O_3, grade III, 20 g) eluting with $CHCl_3$. Final purification by p.l.c. [$CHCl_3$–MeOH (98 : 2)] afforded one major reaction product as an oil (45%); $\nu_{max.}$ 3 600—3 100, 2 970, 2 930, 1 690, 1 445, 1 370, 1 340, 1 250, 1 140, 1 090, 1 030, 940, 900, 890, and 755 cm^{-1}; τ 8.72 (6 H, t, *J* 6 Hz), 8.16 (3 H, s), 7.60 (1 H, br s, exchangeable with D_2O), 5.8 (8 H, m), and 5.1 (2 H, d, *J* 4 Hz); *m/e* 240 (M^+, 3%), 170 (40), 169 (35), 142 (100), 141 (40), 114 (60), 113 (54), 85 (43), 70 (54), and 57 (19) (Found: M^+ 170.104 7. $C_{12}H_{20}N_2O_3 - C_4H_6O$ requires 170.105 5).

2,5-*Diethoxy*-3-(1-*hydroxy*-1-*methylallyl*)-3,6-*dihydropyrazine* (7).—Following the standard procedure, methyl vinyl ketone (0.7 mmol) was condensed with DEDP (0.6 mmol) and the crude product purified by p.l.c. [$CHCl_3$–MeOH (98 : 2)] to give the *title compound* as the major product (47%) as an oil; $\nu_{max.}$ 3 450, 2 970, 1 685, 7 440, 1 370, 1 240, 1 135, 1 085, 1 340, 1 030, 920, and 755 cm^{-1}; τ 8.72 (6 H, t, *J* 6 Hz), 8.60 (3 H, s), 5.9 (7 H, m), and 4.5 (3 H, m); *m/e* 240 (M^+, 0.3%), 226 (2), 170 (28), 169 (7), 141 (9), 113 (8), 87 (9), 85 (67), 83 (100), and 48 (9) (Found: M^+, 240.147 3. $C_{12}H_{20}N_2O_3$ requires *M*, 240.147 4).

2,5-*Diethoxy*-2-(1-*hydroxy*-1-*methylethyl*)-3,6-*dihydropyrazine* (8).—The DEDP (2.9 mmol) was condensed with acetone (2.9 mmol) under the standard conditions, the work-up involving chromatography (Al_2O_3, grade III, 10 g) and p.l.c. [$CHCl_3$–MeOH (98 : 2)]. The *dihydropyrazine* was

obtained as an oil (51%); $\nu_{max.}$ 3 440, 2 970, 2 930, 2 900, 1 685, 1 460, 1 370, 1335, 1 240, 1 140, 1 080, 1 030, 910, 820, 790, and 760 cm^{-1}; τ 8.84 (12 H, m), 6.56 (1 H, exchangeable with D_2O), and 5.96—5.7 (7 H, m); *m/e* 228 (M^+, 3%), 213 (6), 170 (100), 169 (50), 142 (28), 141 (44), 113 (39), and 87 (17) (Found: M^+, 228.146 8. $C_{11}H_{20}N_2O_3$ requires *M*, 228.147 4).

Oxidation and Dehydration of the Dihydropyrazine (8).—The pyrazine (0.42 g, 1.9 mmol) and dichlorodicyanobenzoquinone (0.43 g, 1.9 mmol) were refluxed in dry benzene for 1 h. The mixture was cooled, filtered, and concentrated, and the residue eluted through Al_2O_3 (grade III, 10 g) with light petroleum to afford 2,5-*diethoxy*-3-(1-*hydroxy*-1-*methylethyl*)*pyrazine* (11) as a yellow oil (52%); $\nu_{max.}$ 3 450, 2 970, 1 450, 1 370, 1 335, 1 260, 1 160, 1 095, 1 040, 920, 880, 780, and 750 cm^{-1}, τ 8.84 (6 H, t, *J* 7 Hz), 8.54 (6 H, s), 6.40 (1 H, br s), 5.8 (4 H, m), and 2.40 (1 H, s); *m/e* 226 (M^+, 31%), 211 (100), 183 (62), 155 (46), 137 (23), 93 (15), and 72 (15) (Found: M^+, 226.131 6. $C_{11}H_{18}N_2O_3$ requires *M*, 226.131 7).

When the pyrazine (11) (89 mg) was refluxed in dry benzene for 1 h in the presence of a trace of toluene-*p*-sulphonic acid and molecular sieves, dehydration occurred. After filtering and concentration, the residue was purified by p.l.c. [$CHCl_3$–MeOH (99 : 1)] to give 2,5-*diethoxy*-3-*isopropenylpyrazine* (12), as a yellow oil (80%); $\nu_{max.}$ (film) 2 980, 1 430, 1 380, 1 340, 1 310, 1 190, 1 110, 1 040, 1 030, and 920 cm^{-1}; τ 8.54 (6 H, t, *J* 8 Hz), 7.80 (3 H, s), 5.8—5.6 (4 H, q, *J* 8 Hz), 4.1 (2 H, d, *J* 1.5 Hz), and 2.24 (1 H, s); *m/e* 208 (M^+, 100%), 194 (19), 182 (25), 181 (13), 166 (25), 154 (31), 151 (25), 150 (25), 125 (25), 108 (19), 92 (63), 73 (25), 69 (31), and 57 (69) (Found: M^+, 208.121 4. $C_{11}H_{16}N_2O_2$ requires *M*, 208.121 2).

2,5-*Diethoxy*-3,6-*bis*-(α-*hydroxybenzyl*)-3,6-*dihydropyrazine* (10).—The usual procedure was employed to condense the mono-adduct (5) with a second mole of benzaldehyde. The initial yellow colour of the anion, formed with 2 equiv. of base, was discharged upon addition of the aldehyde. Work-up, as usual, afforded after chromatography (Al_2O_3, grade III), an isomeric mixture of the condensation products (10) as an oil (52%); $\nu_{max.}$ (film) 3 350, 2 980—2 880, 1 685, 1 440, 1 370, 1 350, and 1 250 cm^{-1}; τ 8.7 (6 H, m), 6.4—4.8 (6 H, m), and 3.0—2.7 (10 H, m). The mass spectrum, on the mixture, showed *m/e* 382 (M^+, 0.1%), 274 ([*M* − PhCH_2OH]$^+$, 5), 258 (5), 243 (2), 170 (100), 142 (39), 141 (37), 114 (26), 113 (32), 106 (47), 105 (58), 85 (21), and 77 (58).

2,5-*Diethoxy*-3-(1-*hydroxy*-1-*methylpropyl*)-5-(2-*methylallyl*)-3,6-*dihydropyrazine* (9).—Using the normal procedure, but with 2 equiv. of base, the methylallyldihydropryazine (3) (0.9 mmol) was reacted with ethyl methyl ketone (0.9 mmol) and worked-up as usual. The fluid, pale yellow oil so obtained was chromatographed (Al_2O_3, grade III, 20 g) to give the title compound as a mixture of isomers (61%); $\nu_{max.}$ 3 560, 3 480, 2 980, 2 920, 1 690, 1 440, 1 370, 1 240, 1 140, 1 090, 1 030, and 890 cm^{-1}; τ 9.2—8.6 (14 H, m), 8.3 (3 H, s), 7.55 (2 H, m), 6.1—5.6 (7 H, m), and 5.3 (2 H, m); *m/e* 296 (M^+, 2%), 267 (8), 224 (30), 195 (8), 169 (100), 141 (88), 113 (32), 85 (34), 73 (22), and 53 (44) (Found: M^+, 296.210 2. $C_{16}H_{28}N_2O_3$ requires *M*, 296.210 0).

Dehydrogenations with Dichlorodicyanobenzoquinone (DDQ).—*General procedure*. The dihydropyrazine was heated with DDQ [1 equiv., except for (5), when 2 equiv. were used] in refluxing benzene for 2—16 h, the reactions being monitored by t.l.c. The reaction mixture was filtered and the residue either chromatographed (Al_2O_3, grade III), or subjected to p.l.c. (SiO_2 G), the major products being isolated. In this manner the following compounds were isolated. 2,5-*Diethoxy*-3-*benzoylpyrazine* (14) was the less-polar product from oxidation of (5); obtained as a yellow oil (40%); $\nu_{max.}$ (film) 3 060—2 840, 1 675, 1 597, 1 580, 1 460, 1 380, 1 345, 1 300, 1 165, 1 155, 1 130, 1 090, 1 040, 910, 815, 760, 715, and 700 cm^{-1}; $\lambda_{max.}$ (EtOH) 207, 220, 253, and 329 nm (ε 12 000, 11 000, 5 857, and 5 230 respectively); τ 8.7 (6 H, m), 5.76 (4 H, m), and 2.9—2.2 (6 H, m); *m/e* 272 (M^+, 19%), 243 (12), 149 (12), 122 (11), 105 (100), and 77 (45) (Found: M^+, 272.116 0. $C_{15}H_{16}N_2O_3$ requires *M*, 272.116 1).

2,5-*Diethoxy*-3-(α-*hydroxybenzyl*)*pyrazine* (13) was the more polar product from the oxidation of (5); obtained as an oil (40%); $\nu_{max.}$ (film) 3 600—3 300, 3 100—2 800, 1 440, 1 210, 1 050, 920, 755, and 665 cm^{-1}, τ 8.76—8.48 (6 H, m), 5.8—5.4 (5 H, m), 4.2 (1 H, d, *J* 6 Hz, collapses to a singlet on D_2O exchange), 2.84—2.72 (5 H, m), and 2.44 (1 H, s); *m/e* 274 (M^+, 69%), 246 (51), 217 (14), 169 (100), 141 (33), 105 (31), 83 (20), and 77 (27) (Found: M^+, 274.131 8. $C_{15}H_{18}N_2O_3$ requires *M*, 274.131 7).

2,5-*Diethoxy*-3-(3-*tetrahydropyranyloxypropyl*)*pyrazine* (15) was an oil (83%), b.p. 103 °C at 2 mmHg; $\nu_{max.}$ (film) 2 940, 2 860, 1 630, 1 440, 1 340, 1 260, 1 200, 1 130, 1 115, 1 070, 1 030, and 980 cm^{-1}; $\lambda_{max.}$ (EtOH) 245 and 345 nm (ε 8 750 and 3 125); τ 8.7 (6 H, t, *J* 6 Hz), 8.6—8.4 (6 H, m), 7.94 (2 H, m), 6.7—6.1 (6 H, m), 5.8 (4 H, q, *J* 6 Hz), 5.5 (1 H, br s), and 2.4 (1 H, s); *m/e* 310 (M^+, 9%), 226 (81), 195 (57), 182 (100), 167 (33), 153 (48), 149 (29), 126 (33), 97 (29), 85 (90), 68 (29), and 57 (43) (Found: M^+, 310.189 6. $C_{16}H_{26}N_2O_4$ requires *M*, 310.189 2).

2,5-*Diethoxy*-3-(2-*methylallyl*)*pyrazine* (17) was an oil (80%); $\nu_{max.}$ (film) 2 970, 2 920, 1 460, 1 380, 1 350, 1 310, 1 280, 1 260, 1 215, 1 155, 1 130, 1 090, 1 040, 890, and 740 cm^{-1}; τ 8.60 (6 H, t, *J* 6 Hz), 8.20 (3 H, s), 6.54 (2 H, s), 5.7 (4 H, m), 5.24 (2 H, m), 2.42 (1 H, s); *m/e* 222 (M^+, 100%), 221 (85), 207 (77), 193 (46), 179 (38), 165 (62), 151 (30), 82 (38), and 55 (46) (Found: M^+, 222.136 2. $C_{12}H_{18}N_2O_2$ requires *M*, 222.136 8).

2,5-*Diethoxy*-6-(1-*hydroxy*-1-*methylpropyl*)-3-(2-*methylallyl*)*pyrazine* (18) was an oil (60%); $\nu_{max.}$ 3 460, 2 960, 1 420, 1 380, 1 340, 1 190, 1 090, 1 040, and 890 cm^{-1}; τ 9.3 (3 H, t, *J* 6 Hz) 8.64 (6 H, m), 8.48 (3 H, s), 8.24 (3 H, s), 8.04 (2 H, q, *J* 6 Hz), 6.56 (2 H, s), 5.64 (4 H, m), 5.24 (2 H, m), and 5.10 (1 H, exchangeable with D_2O); *m/e* 294 (M^+, 5%), 266 (32), 265 (100), 237 (29), 222 (35), 221 (31), 207 (27), 193 (19), 165 (21), 82 (18), and 55 (20) (Found: M^+, 294.193 9. $C_{16}H_{26}N_2O_3$ requires *M*, 294.194 3).

2,5-*Diethoxy*-3-(3-*hydroxypropyl*)*pyrazine* (16).—The ether (15) (0.46 g) was stirred with IR-120 ion-exchange resin (H^+ form) (0.26 g) for 3 h at room temperature in ethanol. The slurry was filtered, concentrated, and chromatographed (Al_2O_3, grade III, 10 g); eluting with light petroleum–$CHCl_3$ mixtures afforded the pyrazine (0.08 g, 21%) as an oil; $\nu_{max.}$ 3 500—3 200, 2 990—2 860, 1 580, 1 540, 1 440, 1 380, 1 330, 1 310, 1 270, 1 170, 1 150, 1 130, 1 040, 920, and 880 cm^{-1}; τ 8.62 (6 H, t, *J* 6 Hz), 8.0 (2 H, m), 7.16 (2 H, m), 6.32 (2 H, m), 5.72 (4 H, m), and 2.44 (1 H, s); *m/e* 226 (M^+, 44%), 195 (46), 182 (100), 167 (29), 154 (24), 153 (27), 139 (22), 126 (24), 125 (24), 97 (12), and 57 (17) (Found: M^+, 226.131 4. $C_{11}H_{18}N_2O_3$ requires *M*, 226.131 7).

2,5-*Diethoxy*-5-(1-*hydroxy*-1-*methylpropyl*)-3-(2-*methylallyl*)-3,6-*epidioxy*-3,6-*dihydropyrazine* (19).—The pyrazine (18) (58 mg) was photo-oxidised with polymer-bound Rose Bengal (80 mg) in dichloromethane (10 ml) under a slow

stream of oxygen for 6 h, when all starting material had been consumed. The mixture was filtered to remove the sensitiser, and the filtrate passed through silica gel before concentrating it *in vacuo* to give the peroxide as a yellow oil (quantitative yield); $\nu_{max.}$ (film) 3 540, 2 980, 2 920, 1 720, 1 600, 1 440, 1 380, 1 240, 1 020, and 890 cm^{-1}; τ 9.0 (3 H, t, *J* 6 Hz), 8.72—8.56 (9 H, m), 8.08 (3 H, s), 8.28—7.96 (2 H, m), 7.2 (2 H, m), 5.86—5.72 (4 H, m), and 5.04 (2 H, s); *m/e* 294 ($[M - O_2]^+$, 5%), 265 (100), 237 (20), 222 (43), 221 (38), 207 (29), 193 (20), 165 (20), 128 (14), 110 (12), 84 (20), 83 (25), and 56 (54) (Found: $[M - O_2]^+$, 294.193 9. $C_{16}H_{26}N_2O_3$ requires $M - O_2$, 294.194 3).

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