Pyrazine Chemistry. Part IV.[1] Thermal [1,4] Eliminations from 3,6-Dihydropyrazines

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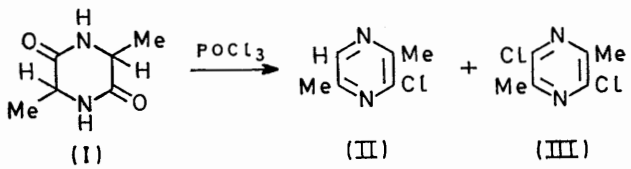
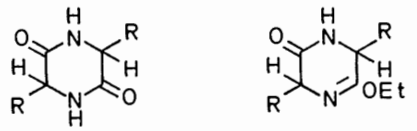
Reaction of piperazine-2,5-diones with an excess of triethyloxonium fluoroborate produced a *cis–trans* mixture of 2,5-diethoxy-3,6-dihydropyrazines which could be oxidised to the corresponding pyrazines in high yield by dichlorodicyanobenzoquinone. *cis*-3,6-Dibenzylpiperazine-2,5-dione reacted with the Meerwein salt to afford a mixture of the *cis*- and *trans*-dihydropyrazines. On pyrolysis, the *trans*-isomer gave 3-benzyl-2,5-diethoxypyrazine in high yield, by elimination of the elements of toluene. Pyrolysis of the *cis*-isomer under the same conditions gave the same products after an initial isomerisation to the *trans*-dihydropyrazine.

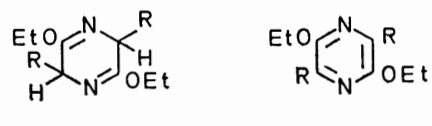
DURING the course of our work on the Diels–Alder reactions of 2,5-dihydroxypyrazines[2] we became interested in developing a convenient synthesis of 2,5-dialkoxypyrazines from piperazine-2,5-diones. Existing methods involved the chlorination of piperazine-2,5-diones with phosphoryl chloride,[3] followed by reaction of the resultant 2,5-dichloropyrazines with sodium alkoxide. The chlorination step is complicated by the fact that mixtures of the mono- and di-chloropyrazines are formed, the former often predominating. Thus, for example 3,6-dimethylpiperazine-2,5-dione (I) gave 3-chloro-2,5-dimethylpyrazine (II) and 2,5-dichloro-3,6-dimethylpyrazine (III) in 60 and 15% yields respectively.[3] The smooth reaction of triethyloxonium fluoroborate with piperazine-2,5-diones[4] suggested a new route to 2,5-diethoxypyrazines, involving oxidation of the initially formed 2,5-diethoxy-3,6-dihydropyrazines.



(I) (II) (III)



(IV) (V)



(VI) (VII)

Treatment of piperazine-2,5-dione[5] (IV; R = H) with an excess † of triethyloxonium fluoroborate in dichloromethane gave 2,5-diethoxy-3,6-dihydropyrazine (VI; R = H) as a solid. Oxidation of compound (VI; R = H) with dichlorodicyanobenzoquinone (DDQ) gave 2,5-diethoxypyrazine (VII; R = H) as an extremely volatile solid. This compound was shown to be a single substance by t.l.c., mass spectral analysis, and ^{1}H n.m.r. spectroscopy.

In a similar manner 3,6-dimethylpiperazine-2,5-dione reacted with an excess of the Meerwein salt yielding the products (V; R = Me) and (VI; R = Me) as crystalline solids. Oxidation of the dihydropyrazine (VI; R = Me) with DDQ gave the pyrazine (VII; R = Me), which was identical to an authentic sample.[6]

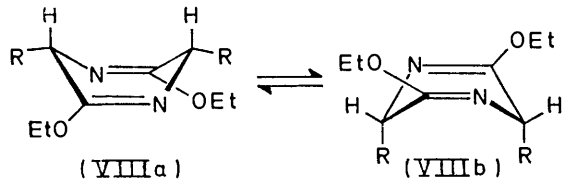
Reaction of *cis*-3,6-dibenzylpiperazine-2,5-dione with the Meerwein salt gave rise to a *cis–trans* mixture of 2,5-dibenzyl-3,6-diethoxy-2,5-dihydropyrazines, which appeared on t.l.c. as two closely running spots. The formation of the isomeric products is indicative of extensive racemisation during the reaction of the piperazine-2,5-dione with triethyloxonium fluoroborate or during the basic work-up, since the piperazine-2,5-dione was formed by the dimerisation of 1-phenylalanine in refluxing ethylene glycol, a process known[7] to give optically pure 3,6-dibenzylpiperazine-2,5-dione. Oxidation of the *cis–trans* mixture (VI; R = CH_2Ph) with DDQ again produced the corresponding pyrazine (VII; R = CH_2Ph) as a crystalline solid.

Separation of the isomeric iminoethers (VI; R = Ph) was achieved by preparative t.l.c. Attempted column chromatography resulted in extensive decomposition. An attempt to microdistil the separated isomers in order to effect further purification resulted in epimerisation, particularly of the minor isomer. The i.r. spectra of the two isomers were virtually identical, differing only in the relative intensities of some of the absorptions. The ^{1}H n.m.r. spectra, however, showed major differences. The major isomer (slower running product on t.l.c.) showed the benzylic protons as the AB part of an ABX spectrum, as a double quartet centred at τ 7·40 (J_{AB} 13, J_{AX} 4 Hz) and 8·00 (J_{AB} 13, J_{BX} 6·5 Hz), with the methine protons buried under the methylene hydrogens of the two ethoxy-groups.

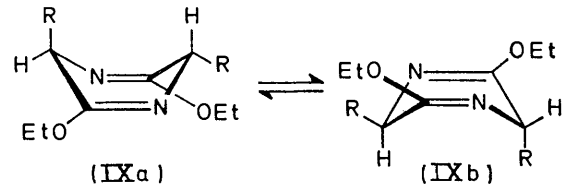
† Use of two equivalents of triethyloxonium fluoroborate usually resulted in a mixture of 5-ethoxy-3,6-dihydropyrazin-2(1*H*)-one (V; R = H) and the diethoxy-compound.

[1] Part I, K. W. Blake and P. G. Sammes, *J. Chem. Soc.* (*C*), 1970, 980; Part II, *ibid.*, p. 1070; Part III, A. E. A. Porter and P. G. Sammes, *ibid.*, p. 2530.
[2] A. E. A. Porter and P. G. Sammes, *Chem. Comm.*, 1970, 1103.
[3] R. A. Baxter and F. S. Spring, *J. Chem. Soc.*, 1947, 1179.
[4] K. W. Blake, A. E. A. Porter, and P. G. Sammes, unpublished observations.
[5] E. Fischer, *Ber.*, 1906, **39**, 2930.
[6] R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1958, 1859.
[7] H. F. Schott, J. B. Larkin, L. B. Rockland, and M. S. Dunn, *J. Org. Chem.*, 1947, **12**, 490; *cf.* K. D. Kopple and G. H. Ghazarian, *ibid.*, 1968, **33**, 862.

Variable temperature studies, from −50 to +50°, showed no change in the pattern observed for the benzylic protons. For the minor isomer the benzylic protons appeared as a doublet at τ 7·16 (J 4 Hz) at



(VIIIa) (VIIIb)



(IXa) (IXb)

+50°. As the temperature was lowered the signal broadened and at −50° appeared as a double AB quartet, the protons centred at τ 6·91 (J_{AB} 13, J_{AX} 3 Hz) and 7·12 (J_{AB} 13, J_{BX} 4 Hz). Thus no sign of frozen conformers [*i.e.* (VIIIa) and (VIIIb)] was observed over the range studied.

Assuming a rapid equilibration of two boat conformers the *trans*-isomer would be equilibrating with an identical conformer (IXa) ⇌ (IXb). Thus, temperature changes would not be expected to alter the ratio of the equilibrating conformers. However, for the *cis*-isomer, the two conformers (VIIIa) ⇌ (VIIIb) are different and hence changes in temperature could alter the equilibrium ratio. On a time averaged basis, therefore, the chemical shift of the benzylic protons for the *cis*-isomer would be expected to change, whereas they should not for the *trans*-isomer. On this argument the major isomer is assigned the *trans*-configuration (IX; R = CH_2Ph). Furthermore, if the two isomers contained a flat dihydropyrazine ring one would expect a similar local environment for the methine and benzylic protons in both cases and hence similar average coupling constants for the ABX systems. The fact that they are not suggests that the rings are in the puckered conformation. Consideration of Dreiding molecular models of the dihydropyrazines (VI) also suggest that they adopt a boat conformation such as (VIIIa or b) for the *cis*-isomer and (IXa or b) for the *trans*-epimer, rather than the virtually planar conformation [8] observed for many of the parent piperazine-2,5-diones. When R ≠ H then the conformer (VIIIa) would be expected to be preferred for the *cis*-isomer because of the reduced 1,4-steric interactions.

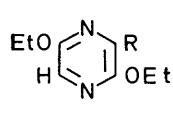
* No attempt was made to find the shortest reaction time necessary to effect this conversion.

[8] *cyclo*-(L-Ala-L-Ala) (Ala = alanine) has a slightly buckled ring with an angle of 26° between the planes of the amido-groups, whereas *cyclo*-(D-Ala-L-Ala) has the expected planar arrangement; C. Benedetti, P. Corradini, and C. Pedone, *J. Phys. Chem.*, 1969, **73**, 2891; *cf.* I. L. Karle, *J. Amer. Chem. Soc.*, 1972, **94**, 81.

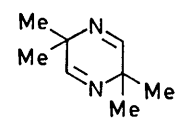
The analogy between (VIII) and (IX) to the cyclohexadiene system suggested that the dihydropyrazines might be capable of undergoing a thermally allowed [9] [1,4] pericyclic elimination, with removal of hydrogen in the case of the *cis*-isomer and of RH in the case of the *trans*-isomer. However, such concerted processes are rare and seem to be limited to molecules in which the eliminated fragment is hydrogen, for example cyclohexa-1,4-diene [10] and 2,5-dihydrofuran.[11] This may be interpreted in terms of orbital overlap in the transition state, since for a concerted elimination to occur, the groups in the 1,4-positions must be sufficiently close for effective overlap to take place. In the case of elimination of hydrogen only 1*s* orbitals are involved, whereas elimination of RH involves the overlap of an *s* orbital with an sp^3 hybrid orbital which requires a specific orientation in space and hence a more ordered transition state. In the case of elimination of R–R, two sp^3 hybrid orbitals have to overlap resulting in an even more ordered and sterically hindered transition state. Thus, from entropy considerations, elimination of R–H or R–R in a concerted manner is probably unfavourable with respect to a free radical reaction.

It was initially decided to examine the pyrolysis of the simplest member of the series, 2,5-diethoxy-3,6-dihydropyrazine (VI; R = H) since only one product *viz* the pyrazine (VII; R = H) is possible. Pyrolysis of compound (VI; R = H) in a sealed tube *in vacuo* for 12 h at 250—270°, resulted in the recovery of unchanged starting material, with no evidence of any elimination product. Increasing the temperature to 350° gave rise to a slight colouration but none of the anticipated pyrazine. At 425° the dihydropyrazine underwent complete decomposition, depositing carbonaceous material on the walls of the reaction vessel, but still giving no sign of the pyrazine (VII; R = H) amongst the elimination products.

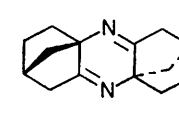
Attention was next directed to the *cis*- and *trans*-2,5-dibenzyl-3,6-diethoxy-2,5-dihydropyrazines as these were available in a pure form. Pyrolysis of the *trans*-compound (IX; R = CH_2Ph) at 250—270° as defined



(X)



(XI)



(XII)

above resulted in the clean formation of 3-benzyl-2,5-diethoxypyrazine (X; R = CH_2Ph) in *ca.* 90% yield along with traces of 2,5-dibenzyl-3,6-diethoxypyrazine (VII; R = CH_2Ph).

Pyrolysis of the *cis*-isomer (IX; R = CH_2Ph) at 250—270° for 12 h * resulted in the formation of the

[9] R. Hoffmann and R. B. Woodward, 'The Conservation of Orbital Symmetry,' Academic Press, New York, 1970.

[10] S. W. Benson and R. Shaw, *Trans. Faraday Soc.*, 1967, **63**, 985.

[11] C. A. Wellington and W. D. Walters, *J. Amer. Chem. Soc.*, 1961, **83**, 4888.

same products as for the *trans*-isomer but in slightly lower yields. No *cis*-elimination of hydrogen was observed. Heating the *cis*-isomer at 120° for longer times resulted in its gradual epimerisation into the *trans*-isomer, whereas under the same conditions the *trans*-isomer remained unaffected, indicating the greater thermodynamic stability of the latter.

Pyrolysis of racemic 3,6-diethoxy-2,5-dihydro-2,5-dimethylpyrazine (VI; R = Me), prepared from *cis*-3,6-dimethylpiperazine-2,5-dione, at 250—270° for 12 h resulted in the formation of a low yield of the pyrazine (X; R = Me). The crude product was contaminated with another component, tentatively assigned as the pyrazine (VII; R = Me), from the ^{1}H n.m.r. spectrum (see Experimental section).

The tetramethyldihydropyrazine (XI), prepared according to the procedure of Rens and Ghosez,[12] which, by analogy with the carbocyclic system,[13] would be expected to eliminate ethane to form 2,5-dimethylpyrazine, gave unchanged starting material on pyrolysis at 250°. At 350° a similar result was observed, whilst decomposition to carbonaceous products occurred at higher temperatures. To date the only other compound of this type to have been examined is the pentacyclic dihydropyrazine (XII) which undergoes [14] an interesting photochemically allowed [9] [1,2] shift, resulting in the racemisation of the optical centres. This compound was reported to be stable to 110—130° but was not pyrolysed above this temperature.

The good yield of the expected product from the pyrolysis of *trans*-3,6-diethoxy-2,5-dibenzyl-2,5-dihydropyrazine suggests that the reaction could be occurring by a concerted [1,4] pericyclic elimination since these processes are usually characterised by high yields,[9] however, since such reactions are rare the alternative mechanism involving radicals is more likely. Since the 2- and 5-positions are doubly allylic, abstraction of a hydrogen atom, either by some site at the wall of the reaction vessel or in a chain reaction, may represent an energetically favourable pathway. The radical intermediate would then be expected to eliminate the resonance stabilised benzyl radical rather than hydrogen, giving the observed product. Failure of the tetramethyldihydropyrazine (XI) and 2,5-diethoxy-3,6-dihydropyrazine (VI; R = H) to give any of the expected products may be explained in terms of the greater difficulty of these molecules to undergo radical-type eliminations.

EXPERIMENTAL

All m.p.s were determined on a Kofler hot-stage and are uncorrected. Pyrolyses were carried out by sealing the sample in a Carius tube at 10^{-2} Torr and heating in a Carius oven, giving a temperature range of ±10°. N.m.r. spectra were determined on a Varian A60 or Varian H.A. 100 spectrometer, using tetramethylsilane as an internal standard. Light petroleum refers to the fraction b.p. 60—80°.

Reaction of Piperazine-2,5-dione with Triethyloxonium Fluoroborate.—Piperazine-2,5-dione [5] (4·25 g) was suspended in dry dichloromethane (25 ml) and a solution of triethyloxonium fluoroborate (13 g, 4 mol equiv.) in dry dichloromethane (20 ml) was added in one portion with stirring, under dry nitrogen, at room temperature. After 3 h a second portion of triethyloxonium fluoroborate (13 g) in dry dichloromethane (20 ml) was added. The mixture was stirred at room temperature for 24 h and then carefully poured onto saturated aqueous sodium hydrogen carbonate solution (50 ml). The dichloromethane layer was separated, washed with water, and dried (Na_2SO_4) before evaporation to yield 2,5-*diethoxy*-3,6-*dihydropyrazine* (4·3 g) as a pinkish solid. This was heated with light petroleum (*ca.* 50 ml) and filtered hot. The filtrate was cooled to give needles (2·02 g) which were sublimed at room temperature at 0·04 Torr, m.p. 84°. $\nu_{max.}$ (Nujol) 1700, 1350, 1250, 1130, 1080, 1030, 930, 915, and 790 cm^{-1}, τ (CCl_4) 8·71 (6H, t, *J* 7 Hz), 5·96 (4H, s), and 5·87 (4H, q, *J* 7 Hz) (Found: C, 56·0; H, 8·0; N, 16·7. $C_8H_{14}N_2O_2$ requires C, 56·5; H, 8·20; N, 16·5%).

Reaction of cis-3,6-*Dimethylpiperazine*-2,5-*dione with Triethyloxonium Fluoroborate.*—3,6-Dimethylpiperazine-2,5-dione (1·5 g) was suspended in dry dichloromethane (25 ml), a solution of triethyloxonium fluoroborate (10 g) in dichloromethane (25 ml) was added, and the mixture was stirred at room temperature under nitrogen. After *ca.* 2 h a clear solution was obtained which was poured onto saturated aqueous sodium hydrogen carbonate (50 ml) and the dichloromethane layer was separated, washed with water, and dried (Na_2SO_4). Evaporation of the dichloromethane gave an off-white solid (1·1 g) which was suspended in light petroleum (20 ml), heated until a clear solution was obtained, and filtered. The filtrate was cooled and the precipitate was filtered and dried to yield 5-*ethoxy*-3,6-*dihydro*-3,6-*dimethylpyrazin*-2(1H)-*one* (0·2 g), m.p. 114—115°, $\nu_{max.}$ (Nujol) 3200, 3050, 1690, 1670, 1320, 1240, 1145, and 1040 cm^{-1}, τ ($CDCl_3$) 8·73 (3H, t, *J* 7 Hz), 8·58 (3H, d, *J* 7 Hz), 5·90 (4H, m, CH_3CH and $CH_3{:}CH_2O$), and 2·1br (1H, s, exchangeable with D_2O) (Found: C, 56·8; H, 8·1; N, 16·1. $C_8H_{14}N_2O_2$ requires C, 56·6; H, 8·2; N, 16·5%).

The filtrate from the extraction was evaporated to dryness and the resultant solid sublimed at room temperature at 0·1 Torr to yield 3,6-*diethoxy*-2,5-*dihydro*-2,5-*dimethylpyrazine* (0·7 g), m.p. 70—71°, $[\alpha]_D^{22}$ 0·0° (*c* 0·5, $CHCl_3$) $\nu_{max.}$ (CCl_4) 3200—2800, 1690, 1490, 1460, 1385, 1345, 1305, and 1220—1260 cm^{-1}, τ ($CDCl_3$) 8·75 (6H, t, *J* 7 Hz), 8·68 (6H, d, *J* 7 Hz), and 5·90 (6H, m, CH_3CH and CH_3CH_2O) (Found: C, 60·0; H, 8·9; N, 14·4%. $C_{10}H_{18}N_2O_2$ requires C, 60·6; H, 9·1; N, 14·2%).

Reaction of cis-3,6-*Dibenzylpiperazine*-2,5-*dione* [15] *with Triethyloxonium Fluoroborate.*—*cis*-3,6-Dibenzylpiperazine-2,5-dione (5 g) was suspended in dry dichloromethane (25 ml) under nitrogen with stirring and a solution of triethyloxonium fluoroborate (6·5 g) in dichloromethane (10 ml) was added in one portion at room temperature. After 16 h a further quantity of triethyloxonium fluoroborate (6·5 g) in dichloromethane (10 ml) was added. After 24 h the reaction was worked-up in the usual way to give a

[12] M. Rens and L. Ghosez, *Tetrahedron Letters*, 1970, 3675.
[13] W. Reusch, M. Russell, and C. Dzurella, *J. Org. Chem.*, 1964, **29**, 2446.
[14] D. G. Farnum and G. R. Carlson, *J. Amer. Chem. Soc.*, 1970, **92**, 6700.
[15] K. Bleiku, *Coll. Czech. Chem. Comm.*, 1969, **34**, 4000.

waxy solid (5·5 g). This solid was triturated with light petroleum, filtered, and the filtrate was evaporated to yield a solid (4·87 g). T.l.c. (SiO_2–$CHCl_3$) showed a mixture of two closely running spots. A sample was sublimed at 90° and 10^{-4} Torr (t.l.c. unchanged) to yield a mixture of the *cis*- and *trans*-iminoethers, m. range 60—61°. The two products were separated by preparative t.l.c. (SiO_2 G–$CHCl_3$) to give the major, more polar trans-2,5-*dibenzyl*-3,5-*diethoxy*-2,5-*dihydropyrazine* (2·21 g), m.p. 76—78°, $\nu_{max.}$ (CCl_4) 3100—3000, 3000—2850, 1690, 1605, 1505, 1490, 1462, 1375, 1355, 1280, 1190, 1145, 1120, 1100, 1085, 1050, and 940 cm^{-1}, τ ($CDCl_3$) 8·78 (6H, t, J 7 Hz), 8·00 (2H, dABq, J_{AB} 13, J_{BX} 6·5 Hz), 7·40 (2H, dABq, J_{AB} 13, J_{AX} 4 Hz), 6·01 (6H, m) (Found: C, 75·3; H, 7·4; N, 7·75. $C_{22}H_{26}N_2O_2$ requires C, 75·4; H, 7·5; N, 8·0%). The minor isomer was cis-2,5-*dibenzyl*-3,5-*diethoxy*-2,5-*dihydropyrazine* (0·44 g), m.p. 59—60°, $\nu_{max.}$ (CCl_4) 3100—3000, 3000—2850, 1690, 1605, 1505, 1490, 1462, 1450, 1375, 1355, 1315, 1280—1220, 1200, 1145, 1102, 1085, and 1047 cm^{-1}, τ ($CDCl_3$, 50°) 8·75 (6H, t, J 7 Hz), 7·16 (4H, d, J 4 Hz), 6·44 (2H, t, J 4 Hz), 5·95 (4H, q, J 7 Hz), and 2·8—3·2 (10H, m) (Found: C, 75·3; H, 7·5; N, 7·8%).

Oxidations with DDQ.—2,5-Diethoxy-3,6-dihydropyrazine (1·0 g) was dissolved in dry benzene (50 ml) and DDQ (1·33 g) was added. The mixture was refluxed for 2 h and allowed to cool overnight. The insoluble quinol was removed by filtration and the filtrate was evaporated to *ca.* 5 ml and passed through alumina (grade III), eluting with benzene. The pale yellow eluate was evaporated to give an oil which solidified on cooling. The product was sublimed at 90° and 0·1 Torr to yield 2,5-diethoxypyrazine as chunky crystals (0·67 g), m.p. 30—31°. $\nu_{max.}$ (CCl_4) 3020, 2978, 2895, 2865, 1470, 1375, 1335, 1260, 1200, 1170, 1155, 1105, 1090, 1040, 1010, 920, 900, and 887 cm^{-1}, τ (CCl_4) 8·65 (6H, t, J 7 Hz), 5·72 (4H, q, J 7 Hz), and 2·37 (2H, s). Although this compound was pure by t.l.c. (SiO_2–$CHCl_3$–acetone, 9 : 1) poor microanalytical figures were consistently obtained due to solvation.

In a similar way 3,6-diethoxy-2,5-dihydro-2,5-dimethylpyrazine (0·1 g) was oxidised with DDQ (0·114 g) in benzene (8 ml). After 30 min at reflux t.l.c. (SiO_2–$CHCl_3$) showed no starting material remained. The mixture was cooled and the quinol filtered, passing the filtrate through a short column of alumina (10 × 1·5 cm of grade III), eluting with benzene. The benzene eluate was evaporated and the residue sublimed at 25° and 0·1 Torr to give 2,5-diethoxy-3,6-dimethylpyrazine (0·054 g), m.p. 77—78° (lit.,[6] 77—78°), $\nu_{max.}$ (CCl_4) 1450, 1415, 1390, 1350, 1265, 1190, 1168, 1100, 1050, 1000, 935, and 680 cm^{-1}, τ (CCl_4) 8·62 (6H, t, J 7 Hz), 7·7 (6H, s), and 5·69 (4H, q, J 7 Hz).

Similarly 2,5-dibenzyl-3,6-diethoxy-2,5-dihydropyrazine (1·0 g) in dry benzene (50 ml) was oxidised with DDQ (0·64 g) to give after work-up as above 2,5-*dibenzyl*-3,6-*diethoxypyrazine* (0·84 g). T.l.c. (SiO_2–benzene) showed this to be slightly contaminated with starting material and thus a portion (0·25 g) was purified by p.l.c., developing with benzene and the isolated product was distilled at 120—130° at 0·1 Torr to yield the pyrazine (0·21 g), m.p. 48—49°, $\nu_{max.}$ (CCl_4) 3055, 3023, 2870, 2820, 1417, 1381, 1347, 1250, 1185, 1160, 1127, 1081, 1067, 1037, 995, and 795 cm^{-1}, τ (CCl_4) 8·68 (6H, t, J 7 Hz) 6·08 (4H, s), 5·72 (4H, q, J 7 Hz), and 2·73 (10H, s) (Found: C, 75·7; H, 6·8; N, 7·8. $C_{22}H_{24}N_2O_2$ requires C, 75·8; H, 6·9; N, 7·7%).

Pyrolysis of trans-2,5-*Dibenzyl*-3,6-*diethoxy*-2,5-*dihydropyrazine.*— *trans*-2,5-Dibenzyl-3,6-diethoxy-2,5-dihydropyrazine (0·05 g × 3) was sealed in a Carius tube at 0·1 Torr and heated at 260° for 12 h. T.l.c. (SiO_2–benzene) showed that no starting material remained and that two products were present. The products were separated by p.l.c. The major product (0·099 g) was microdistilled at 130—140° at 0·1 Torr to give 3-*benzyl*-2,5-*diethoxypyrazine* (0·095 g) as an oil with a slight fluorescence, $\nu_{max.}$ (CCl_4) 3100—2800, 1605, 1505, 1490, 1478, 1450, 1415, 1390, 1357, 1300—1320, 1280, 1220, 1160, 1130, 1100, and 1040—1060 cm^{-1}, τ (CCl_4) 8·7 (6H, t, J 7 Hz), 6·10 (2H, s), 5·82 (2H, q, J 7 Hz), 5·80 (2H, q, J 7 Hz), 2·8—3·0 (5H, m), and 2·58 (1H, s) (Found: C, 69·8; H, 7·3; N, 10·8. $C_{15}H_{18}N_2O_2$ requires C, 69·7; H, 7·0; N, 10·8%).

The minor product (0·007 g.) was identified as 2,5-dibenzyl-3,6-diethoxypyrazine by t.l.c. comparison with an authentic sample (*vide supra*).

Pyrolysis of cis-2,5-*Dibenzyl*-3,6-*diethoxy*-2,5-*dihydropyrazine.*— 2,5-Dibenzyl-3,6-diethoxy-2,5-dihydropyrazine (0·05 g × 3) was sealed in a Carius tube at 0·1 Torr. The tubes were heated in a Carius oven at 260° for 12 h and the mixture was examined by t.l.c. (SiO_2–benzene) which showed no starting material and two products with the same R_F values as the products from the above reaction. The products were separated by p.l.c. (SiO_2–benzene) to give 3-benzyl-2,5-diethoxypyrazine (0·78 g), identical to previously characterised material, and 2,5-dibenzyl-3,6-diethoxypyrazine (0·003 g) with an identical R_F to authentic material.

Pyrolysis of cis-2,5-*Dibenzyl*-3,6-*diethoxy*-2,5-*dihydropyrazine at* 120 °C.—*cis*-2,5-Dibenzyl-3,6-diethoxy-2,5-dihydropyrazine (0·075 g) was sealed in a Carius tube under vacuum at 0·1 Torr and heated at 120° for 3 days. The product on t.l.c. examination (SiO_2–benzene) showed that both *cis*- and *trans*-isomers were present. The mixture was separated by p.l.c. to give starting material (0·034 g) and *trans*-2,5-dibenzyl-3,6-diethoxy-2,5-dihydropyrazine (0·028 g), m.p. 76—78°, exhibiting identical i.r. and n.m.r. spectra to previously prepared material (*vide supra*).

Pyrolysis of cis-3,6-*Diethoxy*-2,5-*dihydro*-2,5-*dimethylpyrazine.*— cis-2,5-Diethoxy-3,6-dihydro-3,6-dimethylpyrazine (0·03 g) was sealed in a Carius tube under vacuum at 0·1 Torr and heated at 260° for 12 h. The resultant product on examination by t.l.c. (SiO_2–$CHCl_3$–Me_2CO, 9 : 1) showed that no starting material remained and that two closely running products had formed. The reaction mixture was purified by p.l.c. extracting both products in the same band (very little separation) to give crude product (0·011 g), $\nu_{max.}$ (CCl_4) 1450, 1415, 1390, 1350, 1265, 1190, 1168, 1100, 1050, 935, and 680 cm^{-1}, τ ($CDCl_3$) 8·68 (6H, t, J 7 Hz), 7·33 (*ca.* 5·5H, s), 7·38 (*ca.* 0·5H, s), 5·76 (4H, q, J 7 Hz), and 2·54 (0·2H, s). The major product was identified by direct spectral comparison with an authentic specimen.

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