Lithiation α to Heteroatoms: Eliminative Ring Fission of Heterocycles

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The behaviour of some heterocycles, having two heteroatoms in a 1,4-relationship, towards lithium di-isopropylamide (LDA) has been examined. The dihydrobenzothiazines (**2a**—**c**) and (**3b**), morpholine (**12**), benzoxazine (**14**), oxathiane (**16**), piperazine (**18**), tetrahydroquinoxaline (**20**), 1,4-dithiane (**25**), and dihydrodioxine (**27**) undergo ready 'eliminative ring fission.' Very marked differences have been observed for unsubstituted and substituted derivatives. Whereas the dibenzoyltetrahydroquinoxaline (**20**) and the dioxine (**27**) readily react to give ring-opened products (**21**) and (**30**) respectively, substituted derivatives (**22**), (**23**), and (**32**) were found to be completely unreactive.

Carbanionic species bearing a formal negative charge adjacent to a heteroatom have recently become exceedingly useful from a synthetic viewpoint;[1] such species have also been considered to be theoretically interesting.[2]

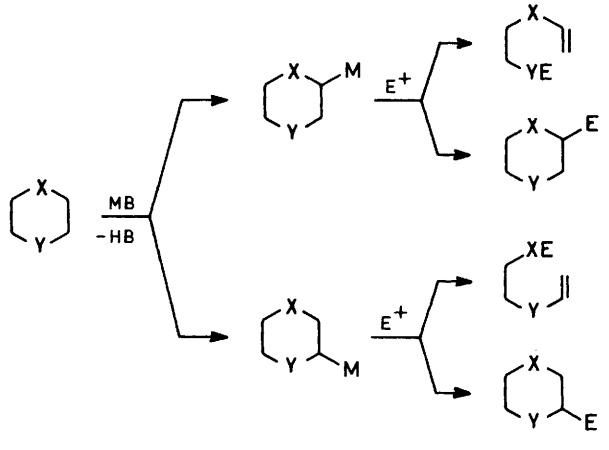
The methodology of such an α-metallation might in principle be applied to promote ring opening of heterocycles. Six-membered ring heterocycles bearing two heteroatoms in a 1,4-relationship such as dihydro-1,4-thiazines, -diazines, -oxazines, 1,4-oxathianes, and 1,4-dithianes are rather reluctant to undergo ring cleavage and specifically 'eliminative ring fission' reactions are quite rare.[3]

We have recently found[4] that some 2,3-dihydro-4*H*-1,4-benzothiazines give 'eliminative ring fission' on treatment with lithium di-isopropylamide (LDA). The reaction turns out to be considerably influenced by the presence of substituents at the 2- or/and 3-position of the heterocyclic ring and may involve either the S–C-2 or N–C-3 bond breaking.

In an effort to gain more insight into the 'eliminative ring fission' of the 1,4-thiazine ring and the factors that govern the direction of the ring-opening reaction, we have prepared some novel 2,3-dihydro-4*H*-1,4-benzothiazine 1-oxides and 1,1-dioxides and investigated their reaction with LDA. Moreover, we have also studied the reaction with LDA of some other heterocyclic systems having two heteroatoms in a 1,4-relationship.

Results and Discussion

In recent years we have been involved in studying the metallation of heterocycles[5] and we reasoned that the methodology of the α-heteroatom metallation might in principle be exploited to promote ring opening of heterocycles bearing two heteroatoms (X and Y) according to the sequence of steps in Scheme 1.

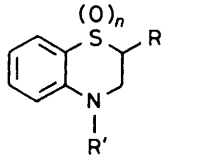


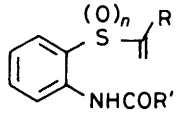
Scheme 1.

According to this sequence metallation might occur α to either X or Y and related metallated intermediates might either be trapped by electrophiles or undergo eliminative ring-fission reaction. Metallation would take place at the α position to X or Y depending on the nature of the heteroatom.[6] The direction of β-elimination would be also dictated by the ability of the heteroatoms X and Y to act as leaving groups.

Reaction of 2,3-*Dihydro*-4H-1,4-*benzothiazine* 1-*Oxides and* 1,1-*Dioxides with LDA.*—In principle two pathways warrant consideration for the eliminative ring fission of dihydrobenzothiazine 1-oxides (**2**) and 1,1-dioxides (**3**): metallation α to sulphur and β-elimination involving C-3–N bond cleavage, and metallation α to the nitrogen atom and subsequent eliminative ring-fission reaction involving the S–C-2 bond breaking. In order to distinguish between these possibilities, the reactions of oxides (**2**) and dioxides (**3**) with LDA were investigated.

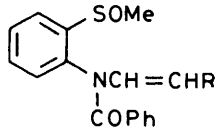
Treatment of the sulphoxide (**2a**) with LDA in tetrahydrofuran (THF) at −78 °C and quenching of the reaction mixture with methyl iodide gave the ring-opened compounds (**4a**) and (**6a**) in a 3:1 ratio (see Table 1).





(**1**) **a**; $n = 0$, R = H, R′ = COPh
b; $n = 0$, R = Me, R′ = COPh
(**2**) **a**; $n = 1$, R = H, R′ = COPh
b; $n = 1$, R = Me, R′ = COPh (*trans*)
c; $n = 1$, R = Me, R′ = COPh (*cis*)
(**3**) **a**; $n = 2$, R = H, R′ = Me
b; $n = 2$, R = Me, R′ = COPh

(**4**) **a**; $n = 1$, R = H, R′ = Ph
b; $n = 1$, R = Me, R′ = Ph
(**5**) $n = 2$, R = Me, R′Ph



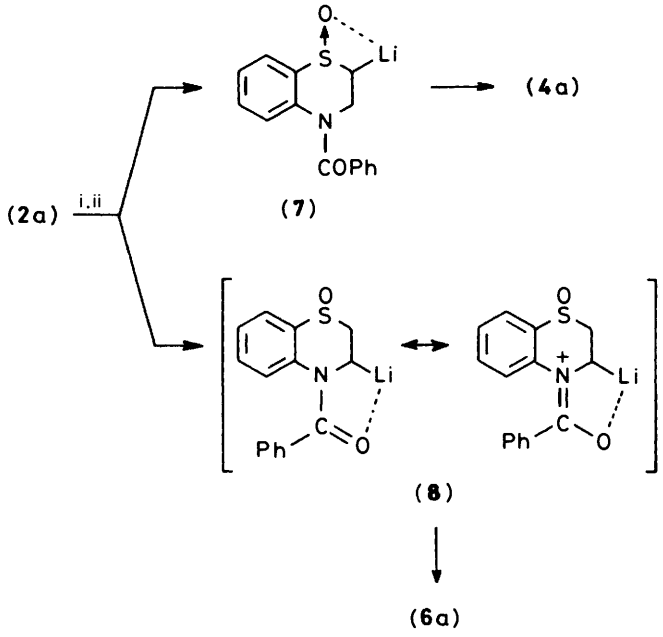
(**6**) **a**; R = H
b; R = Me

Table 1. Ring-opening reaction of heterocycles with LDA in THF

Substrate	Product (%)
(**2a**)	(**4a**) (73), (**6a**) (26), (**9**) (27)
(**2b**)	(**4b**) (10), (**6b**) (16)
(**2c**)	(**4b**) (60)
(**3a**)	No reaction
(**3b**)	(**5**) (67)
(**12**)	(**13**) (80)
(**14**)	(**15**) (89)
(**16**)	(**17**) (75)
(**18**)	(**19**) (76)
(**20**)	(**21**) (86)
(**22**)	No reaction
(**23**)	No reaction
(**24**)	No reaction
(**25**)	(**26**) (68)
(**27**)	(**28**) (52),[a] (**31**) (65)[a]
(**32**)	No reaction

[a] Yield based on the consumed starting material.

It is not unreasonable to assume that the formation of (**4a**) and (**6a**) may involve β-elimination in which the α-sulphinyl lithiated intermediate (**7**) and the 'dipole-stabilised' lithiated species (**8**) may intervene according to Scheme 2. However,

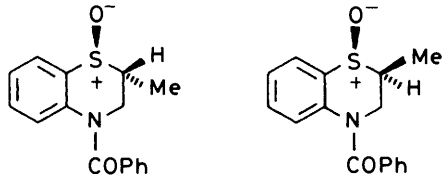


Scheme 2. *Reagents:* i, LDA; ii, MeI

attempted trapping of (**7**) and (**8**) with methyl iodide and deuteriomethanol failed, probably because the β-elimination reactions proceed much faster than methylation and deuteriation. It is noteworthy that the carbamoyl function on one hand provides activation for lithiation α to nitrogen, and on the other behaves as a leaving group in the elimination involving the C-3–N bond rupture.

The reaction of 4-benzoyl-2-methyl-2,3-dihydro-4*H*-1,4-benzothiazine 1,1-dioxide (**3b**) with LDA followed by addition of aqueous ammonium chloride furnished the ring-opened product (**5**) in good yield. Here again lithiation α to the sulphonyl group and subsequent β-elimination may explain the outcome of the reaction. The presence of the benzoyl group on the ring nitrogen is necessary for the ring-opening reaction to take place, as sulphone (**3a**) has been found to be unreactive towards LDA under the experimental conditions in which compound (**3b**) opens.

The oxidation of the dihydrobenzothiazine (**1b**) with *m*-chloroperbenzoic acid (*m*-CPBA) affords a mixture of the diastereoisomeric sulphoxides (**2b**) and (**2c**), which were separated by chromatography and characterized by elemental analysis and n.m.r. spectroscopy. The oxidation has been found to proceed with high stereoselectivity, the *trans* isomer (**2b**) being the main reaction product.



(**2b**) (**2c**)

The structural assignments of *cis–trans* isomers were established on the basis of the chromatographic retention times (R_F) and ^{1}H n.m.r. spectra, including aromatic solvent-induced shifts (ASIS) according to the method used in the configurational assignments of *cis–trans* stereoisomers of the five-membered cyclic sulphoxides bearing an α-methyl group.[7] Indeed, in the case of sulphoxides (**2**) the minor isomer exhibits the larger R_F value on t.l.c. suggesting that in this isomer the sulphoxide oxygen is more sterically hindered and therefore of *cis* geometry, while the major isomer with the smaller R_F value is assigned the *trans* configuration. This structural assignment is also supported by the ASIS studies, which indicated a larger shielding, relative to an inert solvent ($CDCl_3$), of the methine proton in the *cis* isomer, while comparable shieldings are observed for the methyl group at the 2-position (Table 2).

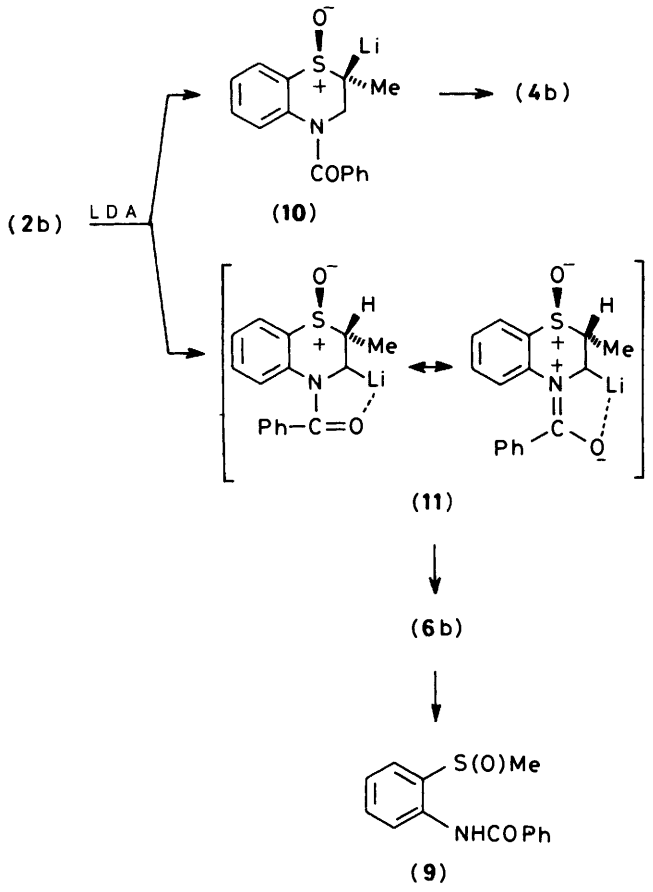
The reaction of *cis* isomer (**2c**) with LDA and quenching with MeI afforded a fair yield of the ring-opened compound (**4b**) as the only 'eliminative ring fission' product. This result was not unexpected in view of the rather strong acidifying effect of the sulphinyl group that favours metallation α to sulphur. Subsequent β-elimination with the carbamoyl group acting as the leaving group would produce (**4b**).

In contrast, the reaction of the *trans* isomer (**2b**) with LDA leads to a mixture of the ring-opened products (**4b**), (**6b**), and (**9**). Lithiation α to the sulphinyl group followed by elimination from the lithiated intermediate (**10**) may explain the formation of (**4b**), while metallation α to nitrogen followed by β-elimination on the 'dipole-stabilised carbanion' (**11**) is likely to be responsible for the formation of (**6b**) according to Scheme 3. Compound (**9**) may derive from compound (**6b**) by a hydrolytic decomposition.* If so, the preferred 'eliminative ring fission' of the heterocyclic moiety in this case is that involving the S–C-2 bond cleavage and this is clearly in contrast with the reaction of the *cis* isomer (**2c**) in which only β-elimination leading to the ring-opened product (**4b**), that is that involving the C-3–N bond rupture, has been observed. These results might tentatively be explained if one assumes that in the *trans* isomer the approach

* The hydrolysis of enamines is well documented: E. J. Stamhuis and W. Maas, *J. Org. Chem.*, 1965, **30**, 2156; W. Maas, M. J. Janssen, E. J. Stamhuis, and H. Wynberg, *ibid.*, 1967, **32**, 1111; P. Y. Sollenberger and R. B. Martin, *J. Am. Chem. Soc.*, 1970, **92**, 4261.

Table 2. Solvent effects in the ^1H n.m.r. spectra of 4-benzoyl-2-methyl-2,3-dihydrobenzothiazine 1-oxides (**2b** and **c**).

Compound	Solvent	δ_{Me}	δ_H	$\Delta_{CDCl_3-C_6D_6}{}^{Me}$	$\Delta_{CDCl_3-C_6D_6}{}^{H}$
trans-(**2b**)	$CDCl_3$	1.52	3.08	0.52	0.65
	C_6D_6	1.0	2.43		
cis-(**2c**)	$CDCl_3$	1.52	3.60	0.56	0.75
	C_6D_6	0.96	2.85		



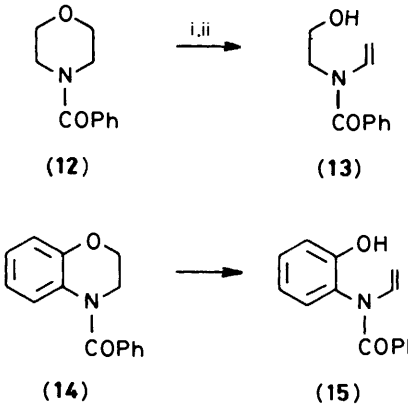
Scheme 3.

of the bulky base (LDA) to abstract the proton α to sulphur is somewhat more difficult for steric reasons (the oxygen atoms and the methyl group could protect the methine proton from being removed) than in the *cis* isomer, so that lithiation α to nitrogen becomes competitive.

Combined with the data previously reported by us[4] the present results clearly indicate that the elimination path of the ring-opening reaction of dihydrobenzothiazines depends on the oxidation state of the ring sulphur, the presence of substituents at the 2- and/or 3-position of the heterocyclic ring, and the presence of a suitable activating group on the nitrogen.

Reaction of Morpholines and Oxathiane with LDA.—In order to gain more information on how the heteroatom may determine the site of metallation and therefore the direction of the 'eliminative ring fission' of heterocycles with two heteroatoms, we examined the behaviour of some morpholines and oxathiane towards LDA.

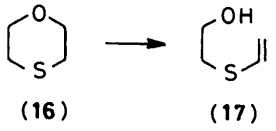
Treatment of *N*-benzoylmorpholine (**12**) with LDA in THF at −78 °C followed by quenching with aqueous NH_4Cl resulted in the clean high-yield formation of the ring-opened product (**13**). Similarly, the reaction of the benzoxazine (**14**) produced a high yield of enamide (**15**).



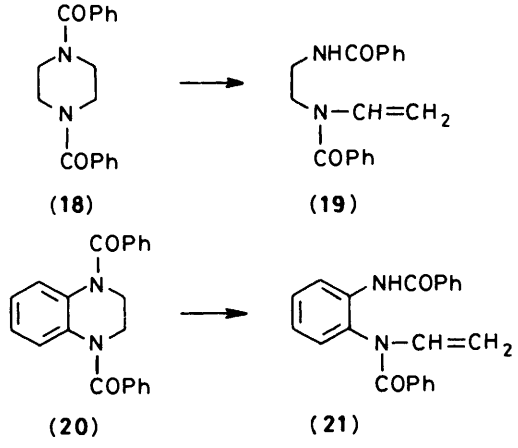
Reagents: i, LDA; ii, H^+

It is not unlikely that the reactions of (**12**) and (**14**) involve lithiation α to nitrogen followed by β-elimination involving the O–C-2 bond breaking. This is in agreement both with the stabilisation provided by the benzoyl group for the metallation α to nitrogen and the propensity of the oxygen at the 1-position for behaving as a leaving group.

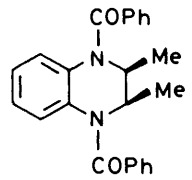
As expected, when oxathiane (**16**) was treated with LDA at 0 °C and MeI was added, 2-vinylthioethanol (**17**) was formed in good yield. This is, indeed, in agreement with the stronger stabilising effect of sulphur for the relative α-carbanion with respect to oxygen.[6]



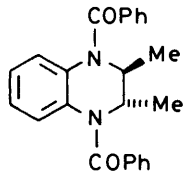
Reactions of Piperazines, Quinoxalines, Dithiane, and Dihydrodioxines with LDA.—When *N,N'*-dibenzoylpiperazine (**18**) and *N,N'*-dibenzoyl-2,3-dihydroquinoxaline (**20**) were treated with LDA in THF at −78 °C and aqueous NH_4Cl was added, a clean ring-opening reaction occurred to provide good yields of compounds (**19**) and (**21**) respectively. Also, in this case, the ring-opening reaction may involve metallation α to nitrogen followed by a β-elimination process.



In contrast, 2,3-dimethylquinoxalines (**22**) and (**23**) underwent no reaction either on treatment with LDA or with Bu^{n}Li–tetramethylethylenediamine (TMEDA), even under more severe conditions (0 °C, long reaction times) than those used for the unsubstituted quinoxaline (**19**).



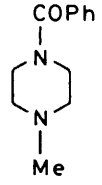
(**22**)



(**23**)

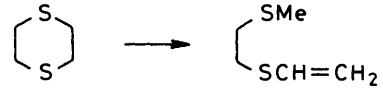
At present it is rather difficult for us to give an explanation for the lack of reactivity of (**22**) and (**23**). However, it may be that steric hindrance around the α-hydrogens could make their removal by the base difficult. Moreover, for steric reasons both (**22**) and (**23**) might have a bias towards a conformation that prevents the carbonyl group from being syncoplanar with the α-C–H bond; this is accepted to be the prerequisite for the α-metallation of carboxamides.[8] Furthermore, there is concrete evidence that in the reaction of amides with LDA or LiTMP* the formation of the amide–lithium complex is crucial for the α-lithiation. Possibly, in the case of (**22**) and (**23**) the appropriate lithium complex does not form or if formed does not have the proper geometry for proton transfer to the di-isopropylamide.†

It is worth mentioning that *N*-benzoyl-*N'*-methylpiperazine (**24**) did not react with LDA; this result supports our suggestion that, on the one hand, the carbamoyl group provides activation for the α-metallation, and on the other promotes β-elimination, acting as a leaving group.



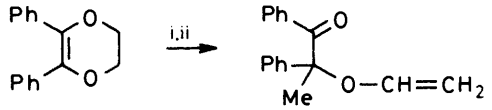
(**24**)

Reactions of 1,4-*Dithianes and* 2,3-*Dihydrodioxines with LDA*.—Having in the same ring, and in a 1,4-relationship, two heteroatoms which may either favour α-metallation or promote β-elimination, 1,4-dithiane (**25**) was expected to give eliminative ring fission. Indeed, treatment of (**25**) with LDA in THF at 0 °C provided the ring-opened product (**26**) after methyl iodide quench. The ability of sulphide to promote α-metallation is well established.[6]



(**25**) (**26**)

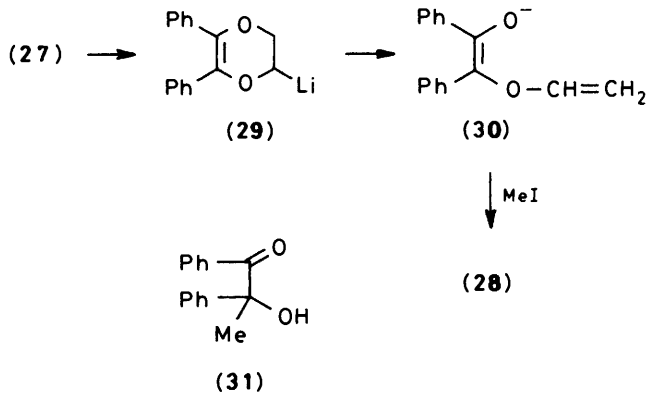
Similarly, the dihydrodioxine (**27**) was ring opened by LDA to give (**28**) even though the conversion was not complete and required rather severe experimental conditions (room temperature, 50 h). It is possible that the reaction involves first



(**27**) (**28**)

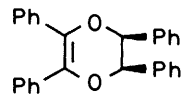
Reagents: i, LDA; ii, MeI

lithiation α to oxygen to give intermediate (**29**); subsequent β-elimination would lead to the enolate (**30**) which is methylated to give (**28**).



(**29**) (**30**) (**31**)

Metallation α to either oxygen is, as is known, rather difficult; in the lithiation of (**27**) the driving force is likely to be provided by the other oxygen in the β position that makes the system activated for the elimination. Despite the presence of the acidic benzylic α-hydrogens, the dihydrodioxine (**32**) has been found to be unreactive towards LDA and Bu^{n}Li–TMEDA. Steric hindrance around the α-hydrogens of (**32**) might render α-hydrogen removal by a bulky base such as LDA difficult.



(**32**)

In conclusion, six-membered heterocyclic systems possessing two heteroatoms in a 1,4-relationship may be ring opened on treatment with LDA. The reaction most probably involves metallation α to one heteroatom and subsequent β-elimination in which the other heteroatom acts as the leaving group. As for dihydro-1,4-benzothiazines the presence of an activating group such as the benzoyl group that provides activation for either the α-nitrogen proton abstraction or the β-elimination involving the C-3–N bond cleavage is necessary. The direction of the eliminative ring fission is dictated by the presence of substituents at the 2- and 3-positions[4] and the oxidation state of sulphur at the 1-position. In the ring fission of morpholines and oxathiane the direction of the elimination is determined by the ability of the heteroatom to provide activation for the α-proton removal (the carbamoyl group and sulphur are stronger than oxygen). Finally, in the heterocyclic systems having two equal heteroatoms the ring fission occurs unless substituents are

* Lithium 2,2,6,6,-tetramethylpiperidide.

† In agreement with the hypothesis that the lack of reactivity of (**22**) and (**23**) may be accounted for in terms of steric factors; n.m.r. evidence shows that they preferentially adopt a half-chair conformation in which the above-mentioned C=O, C–H syncoplanarity is probably not realized (ref. 9).

present at the 2- and 3-positions, in accord with what was observed with 2,3-disubstituted dihydrobenzothiazines.[4] This lack of reactivity may tentatively be explained in terms of steric effects that disfavour the approach of the base and force the carbonyl group (in the case of quinoxalines) not to be syncoplanar with the C–H bond adjacent to the nitrogen.

The present ring cleavage of the above heterocycles may be useful from the synthetic viewpoint as particular enamides, vinyl sulphoxides and sulphones, enol ethers and enol thioethers may be prepared this way. On the other hand our results may contribute toward a better understanding of the reactivity of heterocycles such as benzothiazines, morpholines *etc.*, which are of biological and pharmaceutical interest.

Experimental

M.p.s were determined on a Electrothermal apparatus and are uncorrected. I.r. spectra were taken on a Perkin-Elmer 681 spectrophotometer. ^{1}H n.m.r. spectra were recorded at 60 MHz on a Varian EM 360A instrument, or at 90 MHz on a Varian EM 390 instrument. Chemical shifts are reported as δ units downfield from internal tetramethylsilane. Satisfactory analytical data (± 0.3 for C, H, and N) were obtained for all new compounds.* T.l.c. was performed on silica gel sheets with fluorescent indicator (Stratocrom SIF 254, Carlo Erba); preparative t.l.c. employed Merck 20 × 20 cm (2 mm thickness) plates. Column chromatography was performed on 70—230 mesh silica gel from Merck.

Reactions requiring anhydrous conditions were performed in oven-dried glassware under nitrogen. THF and diethyl ether from commercial sources (Carlo Erba) were purified by distillation (twice) from sodium wire and stored under nitrogen. Commercial Bu^{n}Li (Fluka) was standardized by titration. TMEDA and di-isopropylamine (Fluka) were purified by distillation prior to use. 1,4-Oxathiane, 1,4-dithiane, *m*-CPBA, and [$^2H_6$]DMSO were commerical grade (Fluka). Light petroleum refers to the fraction boiling in the range 40—70 °C.

Compounds (**1a**),[4] (**1b**),[4] (**12**),[10] (**14**),[11] (**18**),[12] (**20**),[9] (**22**),[9] (**23**),[9] (**24**),[13] (**27**),[14] and (**32**)[15] were prepared according to the reported procedures.

4-Methyl-2,3-dihydro-4H-1,4-benzothiazine 1,1-Dioxide (**3a**).—This was prepared by oxidation of 4-methyl-2,3-dihydro-4*H*-1,4-benzothiazine[16] with *m*-CPBA. M.p. 104—106 °C (from EtOH); $\delta_H(CDCl_3)$ 3.0 (3 H, s), 3.2 (2 H, m), 3.85 (2 H, m), and 6.5—7.8 (4 H, m).

4-Benzoyl-2,3-dihydro-4H-1,4-benzothiazine 1-Oxide (**2a**).—*m*-CPBA (27 mmol) in CH_2Cl_2 (130 ml) was added dropwise to a solution of (**1a**) (6.8 g, 27.6 mmol) in CH_2Cl_2 (50 ml) at 0 °C. The reaction mixture was kept at 0 °C for 1 h and then washed in turn with 10% aqueous $Na_2S_2O_3$, 10% aqueous $NaHCO_3$, and water. The CH_2Cl_2 phase was dried over Na_2SO_4 and evaporated under reduced pressure to give a solid residue which was crystallised from CH_2Cl_2–diethyl ether to give *compound* (**2a**) (6.1 g, 84%), m.p. 124—125 °C; $\delta_H(CDCl_3)$ 3.1—4.6 (4 H, complex m) and 6.5—7.7 (9 H, m).

4-Benzoyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine 1-Oxides (**2b** *and* **c**).—To a stirred solution of (**1b**) (3.5 g, 15 mmol) in CH_2Cl_2 (50 ml) was added *m*-CPBA (15 mmol) portionwise at room temperature. After 30 min the resulting precipitate was filtered off and the filtrate was washed in turn with 10% aqueous $Na_2S_2O_3$, 10% aqueous $NaHCO_3$, and water and dried over Na_2SO_4. Evaporation of CH_2Cl_2 left a residue (2.7 g). T.l.c. [light petroleum–ethyl acetate (8:2)] showed the presence of two components which were separated by column chromatography. The first eluted compound (0.3 g, 6.6%), m.p. 146—147 °C (from light petroleum–propan-2-ol) was cis-4-*benzoyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine 1-oxide* (**2c**), $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 7.5 Hz), 3.60 (1 H, m), 4.1 (1 H, dd, *J* 9 and 14 Hz), 4.7 (1 H, dd, *J* 7 and 14 Hz), and 6.65—7.95 (9 H, m). The second eluted material (2.4 g, 54%), m.p. 121—122 °C (from light petroleum–propan-2-ol) was trans-4-*benzoyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine 1-oxide* (**2b**), $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 7.5 Hz), 3.08 (1 H, m, *J* 7.5 and 15 Hz), 4.1 (2 H, m), and 6.7—7.8 (9 H, m).

4-Benzoyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine 1,1-Dioxide (**3b**).—A solution of (**1b**) (4 g, 13.3 mmol) in CH_2Cl_2 (50 ml) was treated with a solution of *m*-CPBA (28 mmol) in CH_2Cl_2 (80 ml) at 0 °C. The reaction mixture was kept at room temperature for 22 h and then washed in turn with 10% aqueous $Na_2S_2O_3$, 10% aqueous $NaHCO_3$, and water and dried over Na_2SO_4. Removal of the solvent under reduced pressure left a solid residue which was crystallised from ethanol to give *compound* (**3b**) (3.6 g, 77%), m.p. 144—145 °C; $\nu_{max.}(CH_2Cl_2)$ 1 670, 1 340, and 1 170 cm^{-1}; $\delta_H(CDCl_3)$ 1.9 (3 H, d), 3.9 (1 H, m), 4.2—5.1 (2 H, m), and 6.6—7.9 (9 H, m).

Reaction of Sulphoxide (**2a**) *with LDA.*—A solution of (**2a**) (1.1 g, 4.1 mmol) in dry THF (30 ml) was added dropwise at −78 °C to a stirred solution of LDA prepared *in situ* (at 0 °C) by adding 1.43M Bu^{n}Li (3.15 ml, 4.5 mmol) to di-isopropylamine (4.5 g, 4.5 mmol) in THF (15 ml). The yellow reaction mixture was treated with excess of MeI and allowed to warm to room temperature. The solution was then treated with aqueous NH_4Cl and extracted with diethyl ether (3 × 20 ml). The organic phase was dried over Na_2SO_4 and the solvent removed under reduced pressure to give an oily residue (1.4 g). T.l.c. (diethyl ether) showed the presence of two compounds which were separated by column chromotography. The first eluted material was *2-benzamidophenyl vinyl sulphoxide* (**4a**) (0.80 g, 73%), m.p. 116—118 °C; $\delta_H(CDCl_3)$ 5.7 (1 H, d, *J* 9 Hz), 5.95 (1 H, d, *J* 16 Hz), 6.55 (1 H, dd, *J* 9 and 16 Hz), 7.0—8.6 (9 H, m), and 10.8 (1 H, brs, exchanges with D_2O). The second eluted component was 2-(N-*vinylbenzamido*)*phenyl methyl sulphoxide* (**6a**) (0.3 g, 26%) as an oil, $\delta_H(CDCl_3)$ 3.4 (3 H, s), 5.9 (1 H, d, *J* 9 Hz), 6.2 (1 H, d, *J* 16.5 Hz), 6.9—7.8 (10 H, m, 9 aromatic protons and 1 vinylic proton).

Reaction of Sulphone (**3b**) *with LDA.*—A solution of sulphone (**3b**) (0.6 g, 2 mmol) in THF (20 ml) was treated with LDA (2.2 mmol) as above. The yellow solution was kept at −78 °C for 30 min and then an excess of MeI was added. After 1 h at room temperature the reaction mixture was treated with aqueous NH_4Cl and extracted with diethyl ether (3 × 25 ml), and the extract was dried over Na_2SO_4 and evaporated under reduced pressure to give a residue that was substantially one product; further purification by column chromatography gave 2-*benzamidophenyl isopropenyl sulphone* (**5**) (0.4 g, 67%), m.p. 78—80 °C; $\nu_{max.}(CH_2Cl_2)$ 3 360, 1 680, 1 310, and 1 160 cm^{-1}; $\delta_H(CDCl_3)$ 1.9 (3 H, s), 5.6 (1 H, s), 6.1 (1 H, s), 7.1—8.8 (9 H, m), and 10.4 (1 H, brs, exchanges with D_2O).

Reaction of Sulphoxide (**2b**) *with LDA.*—To a stirred solution of LDA (1.6 mmol) in THF (10 ml) was added a solution of (**2b**) (0.35 g, 1.25 mmol) in THF (15 ml) at −78 °C. The resulting yellow mixture was quenched with MeI after 1 h at −78 °C and allowed to warm to room temperature. Usual work-up led to a residue (0.3 g) that was a mixture of three components which

* These are available as a Supplementary publication (SUP. No. 23942, 3 pp). For details of the Supplementary Publication scheme, see 'Instructions for Authors (1984),' *J. Chem. Soc., Perkin Trans. 1*, 1984, Issue 1.

were separated by t.l.c. [light petroleum–ethyl acetate (1:1) as developer]. The first eluted material was *2-benzamidophenyl methyl sulphoxide* (**9**) (0.1 g, 27%), $\nu_{max.}(CH_2Cl_2)$ 3 350 and 1 670 cm^{-1}; $\delta_H(CDCl_3)$ 2.9 (3 H, s), 7.1—8.8 (9 H, m), and 11.5 (1 H, brs, slow exchange with D_2O). The second eluted product was the oily *2-benzamidophenyl isopropenyl sulphoxide* (**4b**) (0.04 g, 10%), $\nu_{max.}(CH_2Cl_2)$ 3 350 and 1 680 cm^{-1}; $\delta_H(CDCl_3)$ 1.9 (3 H, s), 5.6 (1 H, s), 6.1 (1 H, s), 7.2—8.8 (9 H, m), and 10.5 (1 H, brs, slow exchange with D_2O). The third eluted component was methyl 2-(*N*-prop-1-enylbenzamido)phenyl sulphoxide (**6b**) (*cis* and *trans*) (0.07 g, 16%) as an oil, $\nu_{max.}(CH_2Cl_2)$ 1 650, 1 600, and 1 050 cm^{-1}; $\delta_H(CDCl_3)$ 1.4 (3 H, d), 2.8 (3 H, s), 5.0 (1 H, m), 6.4 (1 H, m), and 7.1—7.9 (9 H, m).

Reaction of Sulphoxide (**2c**) *with LDA.*—A solution of (**2b**) (0.2 g, 0.7 mmol) in THF (10 ml) was added dropwise to a stirred solution of LDA (0.9 mmol) at −78 °C. Quenching with MeI after 1 h and usual work-up gave a residue (0.16 g). T.l.c. [light petroleum–ethyl acetate (1:1)] indicated the presence of substantially only one product, together with traces of starting material (**2c**). Separation by t.l.c. gave (**4b**) (0.12 g, 60%).

Reaction of N-*Benzoylmorpholine* (**12**) *with LDA.*—A solution of (**12**) (0.5 g, 2.6 mmol) in THF (15 ml) was added dropwise to a stirred solution of LDA (2.8 mmol) in THF (15 ml) at −78 °C. The resulting yellow solution was treated with aqueous NH_4Cl after 1 h, extracted with diethyl ether (3 × 15 ml), and the extracts were dried over Na_2SO_4. Removal of the solvent under reduced pressure gave 2-(N-*vinylbenzamido*)*ethanol* (**13**), purified by column chromatography (diethyl ether as eluant) (0.32 g, 80%) as an oil, $\nu_{max.}(CH_2Cl_2)$ 3 550, 3 440, and 1 660 cm^{-1}; $\delta_H(CDCl_3)$ 3.1 (1 H, brs, exchanges with D_2O), 3.9 (4 H, m), 4.3 (1 H, d, *J* 9 Hz), 4.6 (1 H, d, *J* 15 Hz), 6.6 (1 H, m, *J* 9 and 15 Hz), and 7.4 (5 H, s).

Reaction of the 1,4-*Benzoxazine* (**14**) *with LDA.*—A solution of (**14**) (0.7 g, 2.6 mmol) in THF (15 ml) was treated with a solution of LDA (3.4 mmol) in THF (15 ml) at −78 °C as above. Quenching with NH_4Cl and usual work-up gave 2-(N-*vinylbenzamido*)*phenol* (**15**) (0.63 g, 89%), m.p. 157—159 °C (from EtOH); $\nu_{max.}(CH_2Cl_2)$ 3 560 and 1 660 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 3.9 (1 H, d, *J* 16 Hz), 4.4 (1 H, d, *J* 9 Hz), 6.5—7.7 (10 H, m, 9 aromatic and 1 vinylic proton), and 9.7 (1 H, brs, exchanges with D_2O).

Reaction of 1,4-*Oxathiane* (**16**) *with LDA.*—To a solution of LDA (18.6 mmol) in THF (15 ml) at 0 °C was added a solution of (**16**) (2 g, 17.5 mmol) in THF (30 ml). The resulting yellow solution was quenched with an excess of MeI after 1 h. Extraction with diethyl ether and usual work-up gave a residue (1.72 g) that was substantially one product. Further purification by column chromatography [light petroleum–diethyl ether (8:2)] afforded *2-vinylthioethanol* (**17**) (1.5 g, 75%) as an oil, $\nu_{max.}(CH_2Cl_2)$ 3 500 cm^{-1}; $\delta_H(CDCl_3)$ 2.8 (2 H, m), 3.7 [3 H, m, CH_2 and OH (OH signal exchanges with D_2O)], 5.02 (1 H, d, *J* 16 Hz), 5.11 (1 H, d, *J* 10 Hz), and 6.25 (1 H, dd, *J* 10 and 16 Hz).

Reaction of the Piperazine (**18**) *with LDA.*—A solution of the piperazine (**18**) (0.5 g, 1.7 mmol) in THF (15 ml) was treated with a solution of LDA (1.88 mmol) in THF (15 ml) at −78 °C as above. Quenching with NH_4Cl after 1 h at −78 °C and usual work-up gave N,N′-*dibenzoyl*-N-*vinylethylenediamine* (**19**) (0.38 g, 76%), m.p. 110—112 °C (from EtOH); $\nu_{max.}(CH_2Cl_2)$ 3 380, 1 660, and 1 630 cm^{-1}; $\delta_H(CDCl_3)$ 3.7 (2 H, m), 4.1 (2 H, m), 4.35 (1 H, d, *J* 9 Hz), 4.75 (1 H, d, *J* 14 Hz), 6.6 (1 H, m, *J* 9 and 14 Hz), and 7.1—7.8 (11 H, m).

Reaction of the Dihydroquinoxaline (**20**) *with LDA.*—To a stirred solution of LDA prepared as above (1.7 mmol) in THF (15 ml) was added a solution of the quinoxaline (**20**) (0.5 g, 1.5 mmol) in THF (15 ml) at −78 °C. Addition of aqueous NH_4Cl after 30 min and usual work-up left a residue that was purified by crystallisation from ethanol to give N,N′-*dibenzoyl*-N-*vinyl*-o-*phenylenediamine* (**21**) (0.43 g, 86%), m.p. 130—131 °C; $\nu_{max.}(CH_2Cl_2)$ 3 440, 1 670, and 1 630 cm^{-1}; $\delta_H(CDCl_3)$ 4.25 (1 H, d, *J* 16 Hz), 4.65 (1 H, d, *J* 9 Hz), 6.95—8.5 (16 H, m, 14 aromatic protons, 1 vinylic H, and NH).

Reaction of 1,4-*Dithiane* (**25**) *with LDA.*—A solution of (**25**) (0.5, 4.1 mmol) in THF (10 ml) was added dropwise to a solution of LDA (4.5 mmol) in THF (10 ml) at −50 °C. The yellow solution was kept at −50 °C for 1.5 h and then allowed to warm to room temperature and quenched with an excess of MeI. Usual work-up gave a residue (0.51 g), t.l.c. [methylene dichloride–light petroleum (1:1)] which showed the presence of two compounds which were separated by column chromatography. The first eluted component was S-*methyl*-S′-*vinylethane*-1,2-*dithiol* (**26**) (0.33 g, 68%) as an oil, $\delta_H(CDCl_3)$ 2.1 (3 H, s), 2.8 (4 H, m), 5.03 (1 H, d, *J* 16 Hz), 5.12 (1 H, d, *J* 10 and 16 Hz), and 6.25 (1 H, dd, *J* 10 and 16 Hz). The second eluted component was starting material (**25**) (0.1 g recovery).

Reaction of the 2,3-*Dihydro*-1,4-*dioxine* (**27**) *with LDA.*—A solution of (**27**) (1 g, 4.2 mmol) in THF (15 ml) was added to a stirred solution of LDA (4.6 mmol) in THF (15 ml) at 0 °C. The reaction mixture was allowed to warm to room temperature and was kept there for 72 h. Then an excess of MeI was added. The mixture was stirred for 30 min and then aqueous NH_4Cl was added. Extraction with diethyl ether (3 × 20 ml), drying over Na_2SO_4, and evaporation of the solvent left a residue (1.1 g). T.l.c. [diethyl ether–light petroleum (1:1) as developer] indicated the presence of three components which were separated by column chromatography. The first eluted material was α-*methyl*-α-*vinyloxydeoxybenzoin* (**28**) (0.13 g), $\nu_{max.}(CH_2Cl_2)$ 1 680 and 1 640 cm^{-1}; $\delta_H(CDCl_3)$ 1.8 (3 H, s), 4.1 (1 H, d, *J* 6 Hz), 4.6 (1 H, d, *J* 13.5 Hz), 6.2 (1 H, dd, *J* 6 and 13.5 Hz), and 7.1—7.95 (10 H, m). The second eluted product was starting material (**27**) (0.76 g recovery). The third eluted component was α-*methylbenzoin* (**31**) (0.15 g), $\nu_{max.}(CH_2Cl_2)$ 3 600, 3 450, and 1 670 cm^{-1}; $\delta_H(CDCl_3)$ 1.9 (3 H, s), 4.5 (1 H, s, exchanges with D_2O), and 7.2—8.05 (10 H, m).

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