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New Ring Systems from 1,2-Benzisothiazole-1,1-Dioxides and Related Compounds

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Abstract: Ring-expansions and ring-annulations based on 3-substituted 1,2-benzisothiazole-1,1-dioxides have lead to a variety of novel heterocyclic systems. The reaction of 3-substituted (1H)-1-isoindolones with 1-diethylamino-1-propyne has also resulted in new, ring-expanded molecules in good to modest yields.

The 1,2-benzisothiazole-1,1-dioxide ring system[1] has found a number of useful applications. For example, ring-expansion of 3-bromoalkyl-1,2-benzisothiazole-1,1-dioxides to (2H)-1,2-benzothiazin-4(3H)-one-1,1-dioxides (1)[2] and to 1,2-benzothiazepine-1,1-dioxides (2),[3] have been described. Their flash vacuum pyrolysis leads to benzoxazole derivatives.[4] Condensation of 3-methyl-1,2-benzisothiazole-1,1-dioxide with Danishefsky's diene gave 5a-methyl-5,5a-dihydro-4-oxopyrido[1,2-b]-1,2-benzisothiazoline-1,1-dioxide (3),[5] and that of N-methylsaccharin with N,N-diethyl-1-propynamine gave a spiro-oxete 4.[6] Some of the ring-expanded products have useful biological activity e.g., the benzothiazinone-1,1-dioxides have anti-inflammatory properties (see Piroxicam®, for example[7]), and 3-methyl-1,2-benzothiazepine-1,1-dioxide has anti-convulsant activity.[8]
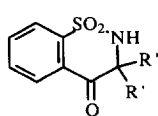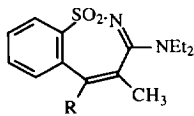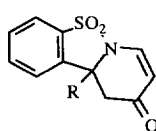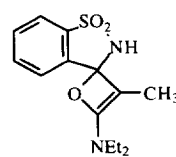
1   2   3   4

We present now a 'pot-pourri' of interesting ring expansions and -annulations of 1,2-benzisothiazoles and related molecules which complement -- or add to -- the above transformations.

3-(β-Phenylvinyl)-1,2-benzisothiazole-1,1-dioxide (5) was synthesized (60% yield) by the decarboxylation of 3-carboxymethylene-1,2-benzisothiazole-1,1-dioxide (6) in benzaldehyde at room temperature, a reaction undoubtedly involving the 3-methylene carbanion.[9] 4-Anisaldehyde behaved similarly,

but the yield of product was very low (5%). Better yields were obtained by adding 3-lithiomethylene-1,2-BID* (**7**) at -20° to -30°C to the aldehydes, followed by the addition of 20% HCl at the same temperature. Thus, **5** (R=H) (80%) and **5** (R=OCH$_3$) (50%) were obtained (kinetic control). On the other hand, if the temperature was raised to room temperature and kept there for 12h *before* acidification, no **5** was obtained. Instead, 3-benzoylmethylene-1,2-BID (**8**) (R=H, 95%; R=OCH$_3$, 50%), presumably owing to thermodynamic control, was formed, as indicated by its IR and NMR spectra ($v_{C=O}$, 1650cm^{-1} α,β-unsaturated ketone; δ 6.82 (s), C=CHCOPh). **5** (R=H) underwent intramolecular Friedel-Crafts alkylation on dissolution in trifluoroacetic acid at R.T. to give the tricyclic system **9** (100%).
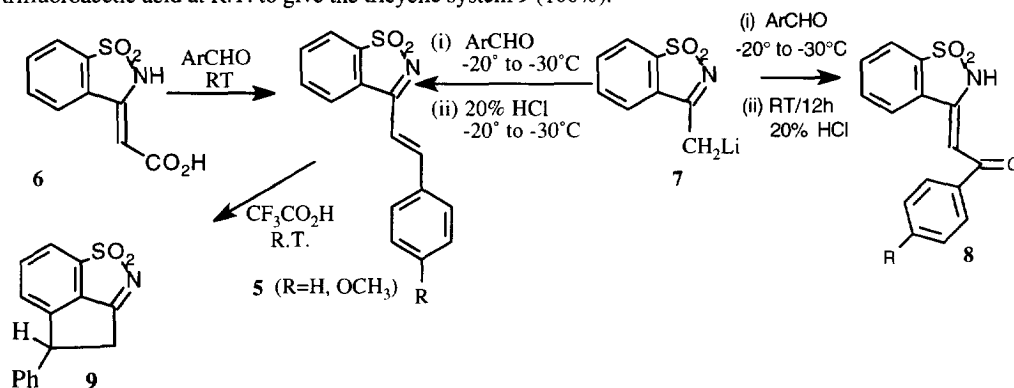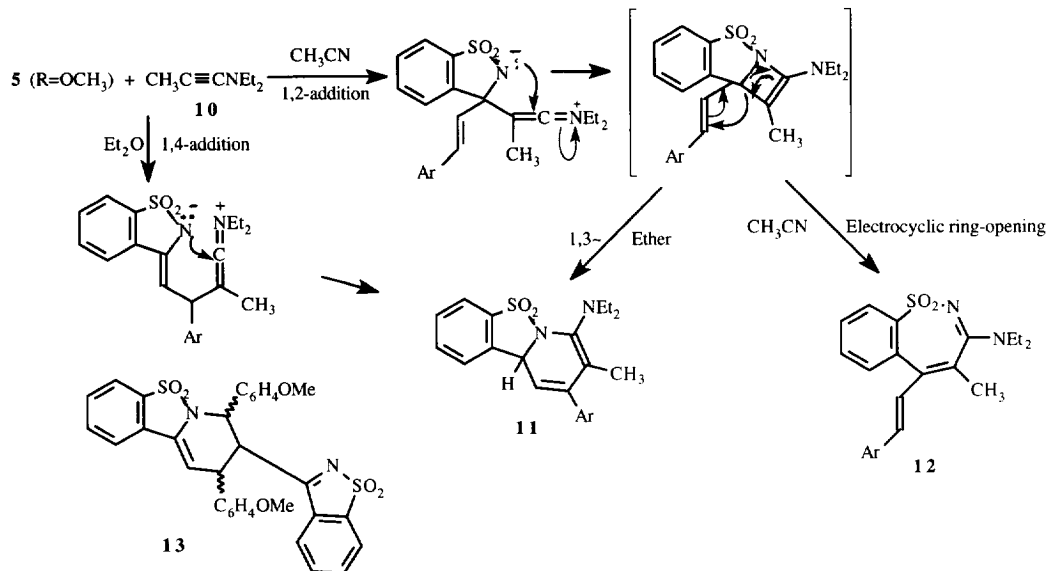

Scheme 1

An interesting solvent effect was observed in the reaction of **5** with 1-diethylamino-1-propyne (**10**). When the reaction was carried out in dry ether solution, rather low yields of the (4+2) adducts (**11**) were obtained (R=H, 19%; R=OCH$_3$, 37%) Structure assignment was relatively straightforward (see spectral data in Exptl. Section). In particular, the 1,2-dihydropyridine structure assignment was made of the basis of a 1H doublet owing to the pyridine C-5 vinylic proton (δ 5.44 - 5.40, J =4Hz), coupled to the benzylic proton at C-2 and the corresponding doublet at δ 4.16 - 4.12 (J = 4Hz) for the C-2 proton. **11** (Ar = Ph) gave a Diels Alder adduct (80% yield) on treatment with 4-phenyl-1,2,4-triazoline-3,5-dione in acetone. Interestingly, when the reaction was carried out with **5** (R=OCH$_3$) in acetonitrile solution, none of adducts **11** were observed; instead, the ring expansion to a thiazepine (**12**) took place in 50% yield (vinyl protons overlap with aromatic protons in the NMR spectrum). One can visualize two possibilities: *either* the ynamine undergoes 1,4-addition in ether and then cyclizes to give **11**, and a 1,2-addition in the more polar acetonitrile, followed by an electrocyclic ring-opening-ring-expansion, *or* the 1,2-adduct is the common intermediate: in Et$_2$O it undergoes a 1,3-sigmatropic shift to give **11**, and in CH$_3$CN it gives **12** *via* the electrocyclic process.

Butadienes are known to add to *N*-tosylimines to form tetrahydropyridines.[10] All attempts to add 2,3-dimethylbutadiene to 3-methoxy- or to 3-tribromomethyl-1,2-BID failed, however, even if anhydrous AlCl$_3$[11] was added. Similar results were obtained with cyclopentadiene. Not unexpectedly, cycloaddition of maleic anhydride or dimethyl acetylenedicarboxylate (DMAD) to **5** (R=OMe) also did not take place, since the

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* BID ≡ benzisothiazole-1,1-dioxide

azadiene **5** is deactivated by the presence of the *N*-sulfonyl group.[12] Aluminum chloride is known to catalyze Diels-Alder additions in which the diene is unreactive.[11]

5 (R=OCH₃) + CH₃C≡CNEt₂

10

CH₃CN, 1,2-addition

Et₂O, 1,4-addition

1,3-, Ether

CH₃CN, Electrocyclic ring-opening

11

12

13

Scheme 2

Reaction of **5** (R = OMe) with DMAD in the presence of AlCl₃ did not give the desired cycloadduct. Surprisingly, one molecule of **5** acted as the dienophile and another as the diene, resulting in the formation of the (4+2)-dimer **13** in 60% yield![13] DMAD did not take part in the reaction.

OSiMe₃

R = CH₃

3 (R = CH₃)

R=Cl

14

16

15
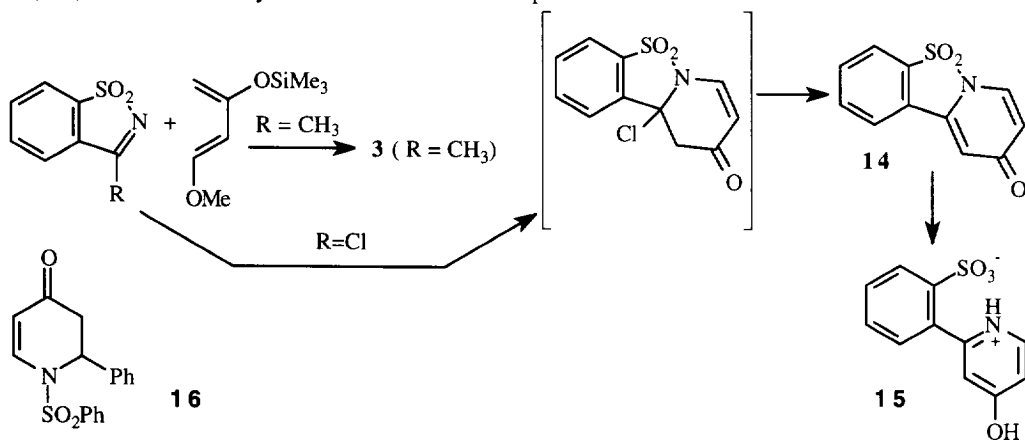
Scheme 3

On the other hand, 3-methyl-1,2-BID reacted with Danishefsky's diene readily, in the absence of a Lewis acid catalyst,[14] to give 5a-methyl-5,5a-dihydro-4-oxopyrido[1,2-*b*]-1,2-BID (**13**; R=Me) (45% yield).[15] 3-Methoxy-1,2-BID did not react, owing possibly to the electron-donating effect of the methoxyl group. On the other hand, saccharin *pseudo*chloride did undergo the cycloaddition and, as expected, HCl

elimination from the intermediate dihydropyridone gave **14** (75% yield), whose structure was confirmed not only by its spectral properties, but also by its facile hydrolysis to the benzenesulfonate **15**. The open chain N-(benzensulfonyl)phenylimine[16] underwent cycloaddition as well to give the dihydro-4-pyridone (**16**) (80%).[15]

It has been reported[17] that treatment of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline with isonicotinoyl chloride and Et₃N gave a spirodihydropyridine in good yield. We have found that heating 3-methyl-1,2-BID with cinnamoyl chloride and 1 eq. of triethylamine in THF for 12h gave the 3,4-dihydro-2-pyridone (**17**) in 60% yield. Oxidation of **17** with DDQ in boiling benzene gave the 2-pyridone (**18**) in quantitative yield.
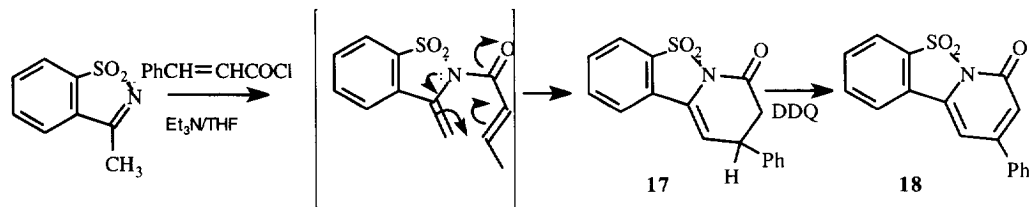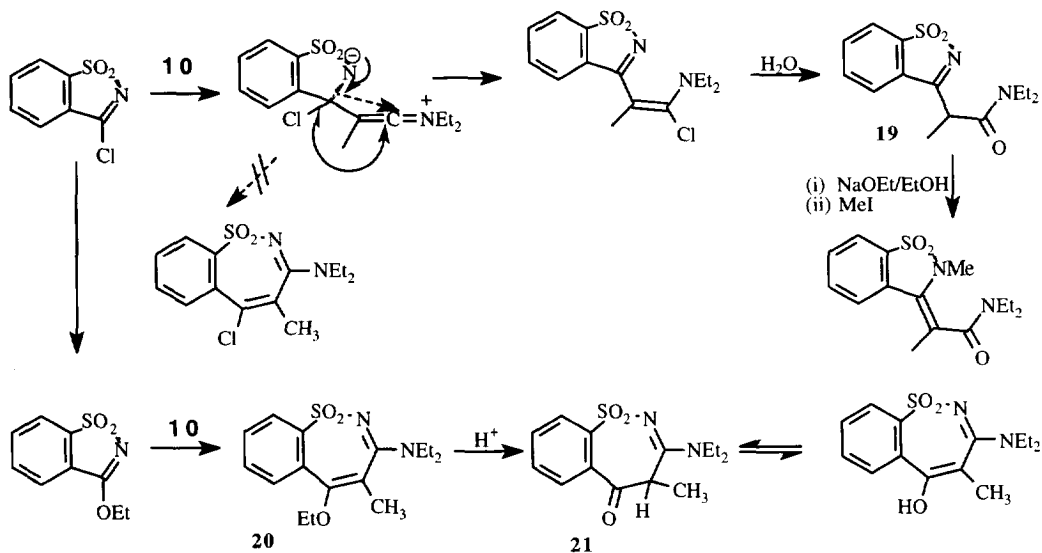

Scheme 4

Saccharin *pseudo*chloride reacted with ynamine **10** to give N,N-diethyl-2-(1,1-dioxido-3-benzisothiazolyl)propionamide (**19**) in good yield; no ring-expansion product was formed. This, and other results, suggests that ynamines add to 1,2-BID derivatives in a stepwise process, and if a good leaving group is present at C-3, it will undergo a 1,3-shift to give a ketene derivative, whereas if the group at C-3 is not as mobile, it is the ring nitrogen that migrates instead to give the thiazepine. Whether an azete intermediate[19] is formed in the present case is uncertain: it is clearly an unnecessary postulate in the system we are discussing. It may, however, have to be invoked in some 3-alkylthio compounds we have been studying.[20] On the other hand, 3-ethoxy-1,2-BID gives exclusively the ring-expanded product (**20**) (91% yield) with no ethoxyl migration. Heating **20** with sulfuric acid under unusually vigorous conditions for an enol ether (12 h, 130°C) gives the expected ketone (**21**) (50%).[3]

We entertained hopes that N-trimethylsilylsaccharin might undergo nucleophilic addition of ynamine **10** to the carbonyl group and that this would be followed by a 1,3-shift of the ring nitrogen (Scheme 5) to give the thiazepine, and this lead to a more direct route to ketone **21**. This hope was only partially fulfilled. Thus, treatment of saccharin with n-BuLi in THF at 0°C, followed by the addition of trimethylsilyl chloride, and then of **10**, still at 0°C gave only a trace of **21**, the 'main' product being **2** (R=Bu) (20.1%), and a small amount of N-methylsaccharin (4.1%). We cannot account for the formation of the latter at present. When the reaction temperature was lowered to -70°C, a 26% of the desired **21** was obtained, together with **2** (R=OSiMe₃) (13.9%). The latter was hydrolyzed quantitatively to **21**. The synthesis of **21** *via* 2-ethoxy-1,2-BID is clearly the superior route, though it does involve more steps. In the solid state, **21** appears to exist as a mixture of the keto and enol forms (IR), but in (CDCl₃) only the keto form can be detected (NMR).

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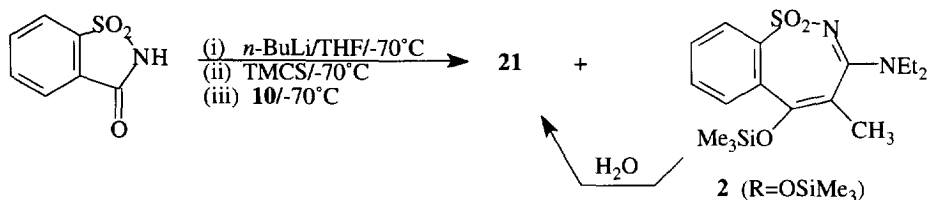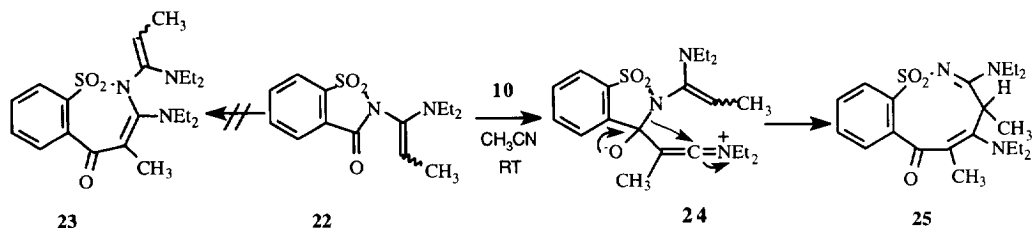

Scheme 5

The direct addition of **10** to saccharin gave the N-substituted derivative (**22**) which, on treatment with a second equivalent of **10**, did not give the expected ring-expansion product (**23**); instead, a compound $C_{21}H_{31}N_3O_3S$ was obtained (28.9%) which is tentatively assigned structure **24** containing a novel 9-membered ring (IR, ^1H and ^{13}C NMR, microanalysis -- the mass spectrum did not show a parent ion).[6] This structure needs confirmation but, to date, a good crystal suitable for X-ray structure determination has not been obtained. A possible route to **24** is sketched in Scheme 6. Structure **24** was eliminated mainly on the basis of the observed v_{co}=1640cm^{-1} (1690cm^{-1} in **8**), the observed methine proton (δ 4.0) as compared with δ 4.9 for that in **22**, but most importantly from the fact that **24** was stable towards mild hydrolytic conditions, whereas **22** regenerates saccharin under these conditions, so that **23** would have been expected to give **21**. A product (27%) which appears to be the chloro-derivative of **24** was also obtained from 6-chlorosaccharin.[20b]

Scheme 6

We now turned to the ring-expansion of the analogous isoindolone derivatives (SO$_2$ replaced by C=O). Thus, 3-ethoxy-(1H)-1-isoindolone (**25**) gave the ring-expanded 2-benzazepin-1-one (**26**; R=OEt) (42% yield) on treatment with **10** at room temperature (Scheme 7). Other 3-substituted (1H)-1-isoindolones are not readily available.   Chlorthalidone (the hydrated form of 3-(4-chloro-3-sulfonamido)phenyl-(1H)-1-isoindolone) is a known diuretic and anticonvulsant.[22] Our attempts to synthesize 3-(4-chlorophenyl)-(1H)-1-isoindolone from 3-n-butoxy-3-(4-chlorophenyl)-2,3-dihydroisoindolone (using a general procedure described by Ben Ishai and Warshawsky[22]) failed. We were able to generate 3-phenyl-(1H)-1-isoindolone in situ from the 3-n-butoxy-dihydro compound either using thionyl chloride or by heating under vacuum at 140°C in a Kugelrohr apparatus. Addition of **10** then gave **26** (R=Ph) (51%).
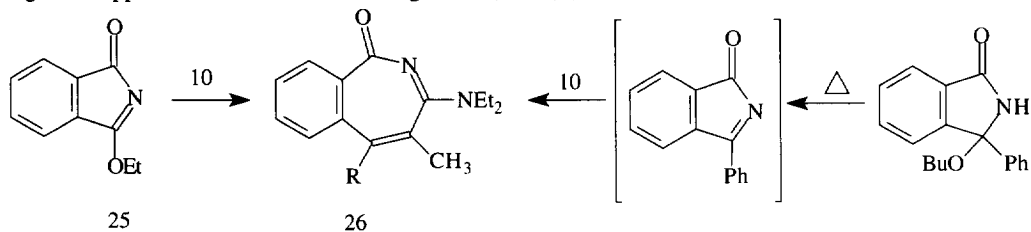
Scheme 7

An alternate route to **26** (R=Ph) was sought, but proved much more complicated.   Thus, N-trimethylsilylphthalimide was treated with PhLi in THF in the expectation that lithium trimethylsiloxide would be eliminated to give 3-phenyl-(1H)-1-isoindolone. Based on our previous experience, the latter was not isolated; instead **10** was added to the reaction mixture subsequently and the mixture heated. A complex mixture of products resulted (Scheme 8), only a small fraction of which was **26** (R=Ph) (8.2%).

Two isomers, C$_{21}$H$_{24}$N$_2$O$_2$, were isolated in low yield and were assigned the diastereoisomeric structures **29** and **30**. These would result from a spirooxete intermediate formed by the addition of **10** to the carbonyl group, followed by ring-opening, and then hydrolysis and a 1,3-H shift. The structural assignments are based on the fact that one isomer (**30**) appears to be intramolecularly hydrogen-bonded (such hydrogen bonding in **29** would require the methyl group to get quite close to H$_7$ of the benzene ring): the OH group of **29** would then be capable of intermolecular hydrogen bonding, which would account for the melting point of **29** being appreciably higher than that of **30**. In solution, the proton resonates at δ 9.1 for **30** and 8.2 for **29**.
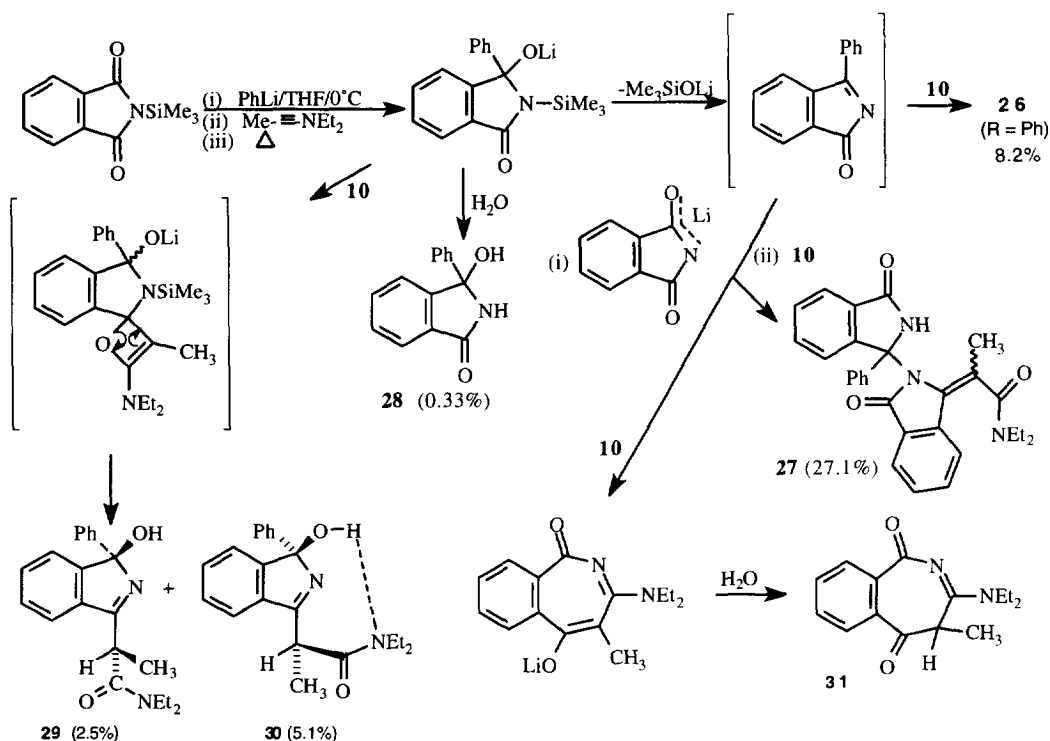
Scheme 8

Otherwise, the mass spectral fragmentations and ^{13}C NMR spectra of the isomers are almost identical. Compound **27** would result from the nucleophilic addition of lithiophthalimide (**32**) (cleavage of *N*-trimethylsilylphthalimide) to the intermediate 3-phenyl-(1*H*)-1-isoindolone followed by addition of ynamine to a carbonyl group (*via* a spirooxete?). If the reaction was carried out in ether solution (lower b.p.) only **27** (14.6%), **29** (14.2%) and **30** (20.9%) were isolated. The proposed mechanism for the formation of **27** was confirmed by the addition of **10** to *N*-methylphthalimide in boiling acetonitrile, which resulted in the exclusive formation of *E*-2-methylisoindol-3(2*H*)-ylidene-2-(*N,N*-diethyl)propionamide (**32**), whose structure and geometry were confirmed by single crystal X-ray analysis (Fig. 1). Interestingly, the amide carbonyl group is almost orthogonal to the plane of the π-system (Fig. 2), thus preventing a steric interaction with H$_7$ of the benzene ring.

On the other hand, the addition of PhLi followed by 2 equivalents of **10** to *N*-trimethylsilylphthalimide was carried out in hot THF a low yield (5.6%) was obtained. This may be formed as in **Scheme 8**. When **28** was heated with 3 equivalents of **10, 29** (22.3%) and **26** (8.8%) were isolated. Clearly, the synthesis of **27** outlined in **Scheme 7** is the preferable one.
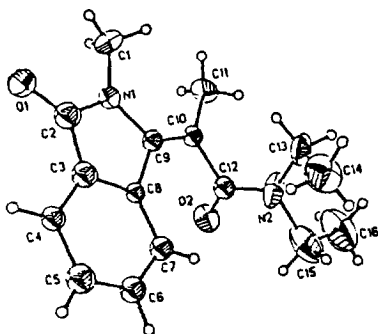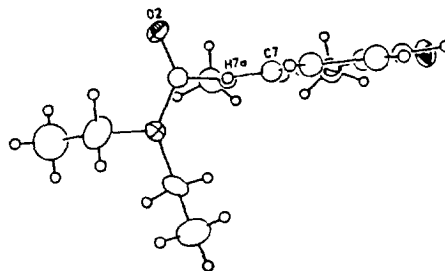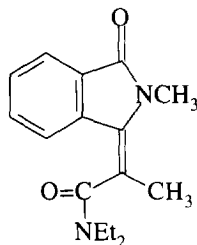
Fig. 1. ORTEP Drawing of Compound **32**.

Fig. 2. Alternate ORTEP Drawing of Compound **32**.

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EXPERIMENTAL

^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra at 50 MHz. Mps are uncorrected.

3-Dicarbethoxymethylene-1,2-benzisothiazole-1,1-dioxide. A solution of saccharin *pseudo*chloride[23] (2.0g, 10 mmole) and diethyl sodiomalonate (2.7g, 15 mmole) in dry benzene (200 ml) was boiled under reflux for 24 h. The solvent was evaporated *in vacuo* and the residue treated with cold 20% hydrochloric acid (100 ml). Filtration gave the desired product, mp 165°C (from absolute ethanol) (3.2g, 100%): IR (KBr) 3180 (NH), 1710, 1690 (C=O), 1330 and 1250cm^{-1} (SO$_2$); ^{1}H NMR (CDCl$_3$) δ 8.0 - 7.66 (m, 4H, ArH), 4.5 - 4.22 (m, 4H, -OCH_2CH$_3$), 1.46 - 1.22 (m, 6H, OCH$_2$CH_3); MS *m/z* (rel. intensity) 325 (M$^+$, 13), 280 (M$^+$-CH$_3$CH$_2$O, 55), 253 (M$^+$-C$_2$H$_4$, -CO$_2$, 48), 208 (M$^-$-C$_2$H$_4$, -CO$_2$, -OCH$_2$CH$_3$, 15), 207 (M$^+$-C$_2$H$_4$, -CO$_2$, -CH$_3$CH$_2$OH, 100), 181 (82), 166 (17), 151 (39), 115 (61), 103 (61), 1002 (61), 89 (39), 88 (61), 77 (39), 76 (74). *Anal.* Calcd. for C$_{14}$H$_{15}$NO$_6$S: C, 51.35; H, 4.61. Found: C, 51.08; H, 4.64.

3-(β-Phenylvinyl)-1,2-benzisothiazole-1,1-dioxide and 3-Phenylindano-7,1-sultim.
(i) The above malonate (3.25g,10 mmole) was treated with 2N NaOH (200 ml) and the resulting yellow solution was stirred at room temperature for 48 h. It was then cooled to 0°C and acidified by the dropwise addition of ice-cold 20% HCl. The precipitate was filtered and dried to give 3-carboxymethylene-1,2-benzisothiazole-1,1-dioxide (**6**) (2g, 100%). IR (KBr) 3280 (NH), 1680 - 1650 (C=O), 1330 and 1260cm^{-1} (SO$_2$). It decomposed to 3-methyl-1,2-BID on attempted recrystallization. A suspension of the carboxylic

acid (1.12g) in freshly distilled benzaldehyde (7.5 ml) was stirred at RT for 12 h. Excess benzaldehyde was distilled under vacuum leaving behind bright yellow 3-(β-phenylvinyl)-1,2-benzisothiazole-1,1-dioxide (**5**; R=H) (0.8g, 60%) which was washed with ether and recrystallized from ethanol: mp 245-247°C; IR (KBr) 1630 (C=C), 1600 (C=N), 1330 and 1170cm⁻¹ (SO₂); m/z (rel. intensity) 269 (M⁺, 10), 268 (M⁺-H, 20), 205 (-SO₂, 50), 204 (-SO₂, -H, 100), 103 (C₆H₅CN⁺, 20), 102 (33), 77 (50), 76 (33), 51 (35), 50 (33). *Anal.* Calcd. for $C_{15}H_{11}NO_2S$: C, 66.92; H, 4.09. Found: C, 66.80; H, 4.21.

A solution of the phenylvinyl compound (2g, 7.4 mmole) in trifluoroacetic acid (20 ml) was stirred for 6h at RT and the poured into ice-cold ether (50 ml). The sultim (**9**) (2g, 100%) precipitated and was recrystallized from acetone-ethanol (1:1, v/v): mp 251-253°C; IR (KBr) 1600 (C=N), 1330 and 1185cm⁻¹ (SO₂); m/z 269 (M⁺, 24), 268 (44), 205 (-SO₂, 68), 204 (100), 103 (12), 102 (20), 77 (24), 76 (14), 51 (12), 50 (10). *Anal.* Calcd. for $C_{15}H_{11}NO_2S$: C, 66.92, H, 4.09. Found: C, 66.81, H, 4.15).

(ii) To a solution of LDA [2.64g, 25 mmole, prepared from diisopropylamine (2.5g, 25 mmole) and *n*-butyllithium (1.6g, 25 mmole)] in dry THF (20 ml) at -30°C under dry nitrogen was added a solution of 3-methyl-1,2-BID (3.6g, 20 mmole) in dry THF (120 ml) dropwise for 1.5h so that the temperature remained at -30°C. A solution of benzaldehyde (2.1g, 20 mmole) in dry THF (20 ml) was then added dropwise over 10 min, and the resulting yellow solution was stirred at -30°C for a further 5 h, and hydrolyzed by the slow addition of a saturated aqueous solution of ammonium chloride to the mixture kept at -30°C. The mixture was then extracted with chloroform (5 x 40 ml), the extracts dried (Na₂SO₄) and the CHCl₃ evaporated to yield **5** (R=H) (4.32 g, 80%), mp 245-247°C (EtOH), identical with that prepared as above.

3-Benzoylmethylene-1,2-benzisothiazoline-1,1-dioxide (8: R=H).

3-Lithiomethyl-1,2-BID was prepared as under (ii) above at -30°C. After stirring at -22°C for 1.5h a solution of benzaldehyde (5.3g, 50 mmole) in dry THF (20 ml) was added dropwise and the resulting yellow solution was stirred at -22°C for 2h and then at room temperature for 12h before hydrolysis at room temperature. **8** (R=H) precipitated and was recrystallized from absolute ethanol to give the ketone (5.4g, 95%), mp 244-245°C. IR (KBr) 3210 (NH), 1650 (C=O), 1600 (C=C), 1330 and 1230cm⁻¹ (SO₂); NMR (CDCl₃/CF₃CO₂H) δ 8-7.4 (m, 10H, aromatic H), 6.82 (s, 1H, =CH-CO); m/z (rel. intensity) 285 (M⁺, 30), 284 (66), 257 (10), 222 (10), 221 (M⁺-SO)₂, 52), 220 (100), 208 (18), 193 (18), 166 (C₆H₄CNSO₂, 16), 165 (20), 105 (PhCO⁺, 56), 102 (16). *Anal.* Calcd. for $C_{15}H_{11}NO_3S$: C, 63.18; H, 3.86. Found: C, 63.16; H, 3.93. It formed an *N*-acetyl derivative (44%), mp 176-178°C, with boiling acetic anhydride. IR (KBr) 1770 (C=O), 1620cm⁻¹ (C=O), m/z 327 (M⁺, 10), 220 (-CH₃CO, -SO₂, 100). *Anal.* Calcd. for $C_{17}H_{13}NO_4S$: C, 62.39; H, 3.98. Found: C, 62.43; H, 4.04.

Reaction of 3-Lithiomethyl-1,2-BID with 4-Anisaldehyde.

a. At -30°C. A solution of 3-lithiomethyl-1,2-BID, prepared as above at -30°C was added dropwise to a solution of 4-anisaldehyde (2.72g, 20 mmole) in dry THF (10 ml) at -30°C. The solution was then stirred at -30°C for 5 h, and hydrolyzed with cold 20% HCl (50 ml). Extraction with CHCl₃ (4 x 30 ml), and evaporation of the dried (Na₂SO₄) extract gave an oil which, on trituration with ethyl acetate (5 ml), gave **5** (R=OMe) (3g, 50%), mp 229-232°C (from EtOH). IR (KBr) 1620 (C=C), 1590 (C=N), 1315 and 1170cm⁻¹ (SO₂); m/z (rel. intensity) 299 (M⁺, 66), 236 (50), 235 (-SO₂ 20), 234 (-SO₂, -H, 100), 220 (-CH₃, -SO₂,

56), 204 (OCH_3, $-SO_2$, 62), 191 (52), 169 (29). *Anal.* Calcd. for $C_{16}H_{17}NO_3S$: C, 64.21; H, 4.35. Found: C, 64.03; H, 4.43. This compound was identical to that obtained from **6** and 4-anisaldehyde at R.T. for 40h: mp 230-231°C (3%).

b. At Room Temperature. This was carried out as for **8** (R=H) above, to give 3-(4-anisoyl)methylene-1,2-benzisothiazoline-1,1-dioxide (**8**; R=OCH_3) (2g, 65%), mp 251-253°C (EtOH); *m/z* 315 (M $^{+}$, 9) 236 ($-SO_2$, -CH_3 15), 135 ($CH_3OC_6H_4CO^{+}$, 90), 107 ($CH_3OC_6H_4^{+}$, 31), 92 (60), 77 (100). Anal. Calcd. for $C_{16}H_{13}NO_3S$: C, 60.95; H, 4.44. Found, C, 60.88; H, 4.19.

Reaction of 5 with 10.

a. In Ether. To a suspension of **5** (R=OCH_3) (0.9g, 3 mmole) in anhydrous ether (50 ml) was added dropwise as solution of 1-diethylamino-1-propyne (**10**) (330 mg, 3 mmole) in anhydrous ether (5 ml) over a period of 5 min. The reaction mixture was stirred at R.T. for 3 h, unchanged **5** (380 mg, 42%), was filtered and the filtrate was concentrated under reduced pressure. Absolute ethanol (5 ml) was added to the residual red oil, and the solution cooled in an ice-salt bath. Crystalline 2-diethylamino-3-methyl-4-(4-anisyl)-1,4-dihydropyrido[1,2-*b*]-1,2-benzisothiazole-1,1-dioxide (**11**) (450 mg, 37%), mp 159-160°C (EtOH), was obtained. IR (KBr) 1630, 1600, 1500, 1450, 1310, 1210, 1170, 830 and 760cm^{-1}; NMR ($CDCl_3$) δ 7.76-7.10 (m, 6H), 6.92-6.76 (d, 2H), 5.42-5.38 (d, 1H, *J*=4Hz, =C*H*-CH-Ar), 4.08-4.04 (d, 1H, *J*=4Hz, =CH-C*H*-Ar), 3.74 (s, 3H, OCH_3), 3.30-3.0 (m, 4H), 1.44 (s, 3H, CH_3), 1.30-1.16 (t, 6H, CH_2CH_3); *m/z* (rel. intensity) 410 (M $^{+}$, 40), 409 (100), 394 (11), 349 ($-OCH_3$, $-C_2H_5$, -H, 18), 330 ($-SO_2$, -CH_3, -H, 30), 317 (18), 316 ($-SO_2$, $-C_2H_5$, -H, 65), 303 (18), 275 (23), 274 (30), 260 (75), 221 (21). *Anal.* Calcd. for $C_{23}H_{26}N_2O_3S$: C, 67.32; H, 6.38. Found: C, 67.24; H, 6.38.

A similar reaction with **5** (R=H) gave **11** (Ar=C_6H_5) (19%), mp 188-189°C (EtOH). NMR ($CDCl_3$) δ 7.8-7.2 (m, 9H, Ar*H*), 5.44-5.4 (d, 1H, *J*=4Hz, =C*H*-CHAr), 4.16-4.12 (d, 1H, *J*=4Hz, =CH-C*H*Ar), 3.3-3.02 (m, 4H, NC*H*$_2$CH$_3$), 1.46 (s, 3H, CH_3), 1.23 (t, 6H, *J*=6Hz, NCH$_2$C*H*$_3$); *m/z* 380 (M $^{+}$, 8). *Anal.* Calcd. for $C_{22}H_{24}N_2O_2S$: C, 69.47; H, 6.32. Found: C, 69.32; H, 6.36. This gave a Diels-Alder product (80%), mp 110°C when treated with 4-phenyl-1,2,4-triazoline-3,5-dione in acetone.

b. In Acetonitrile. To a solution of **5** (R=OCH_3) (0.9g) in dry acetonitrile (50 ml) at 0-5°C was added dropwise a solution of **10** (330 mg) in the same solvent (5 ml). The solution was stirred at 0-10°C from 5 min then at room temperature for 10 min, the solvent was evaporated *in vacuo*, absolute ethanol (5 ml) was added to the gummy residue, and the solution kept in a freezer at -5°C. Product **12** precipitated out and was filtered and recrystallized from absolute ethanol (600 mg, 50%), mp 110-112°. IR (KBr) 1600 (C=N), 1395 and 1160cm^{-1} (SO_2); NMR ($CDCl_3$) δ 8.10-8.00 (m, 1H, Ar*H peri* to SO_2), 7.5-6.6 (m, 9H, Ar-H + 2 vinylic protons), 3.74 (s, 3H, OC*H*$_3$), 3.4-3.0 (m, 4H, NC*H*$_2$CH$_3$), 2.26 (s, 3H, C*H*$_3$), 1.2-1.0 (m, 6H, NCH$_2$C*H*$_3$); *m/z* (rel. intensity) 410 (M $^{+}$, 20), 314 ($-SO_2$ -OCH_3, -H, 46), 260 (35), 236 (21), 210 (28) 207 (42), 194 (49), 186 (35), 181 (100), 149 (56), 135 (90), 117 (49), 103 (56). *Anal.* Calcd. for $C_{23}H_{26}N_2O_3S$: C, 67.32; H, 6.38. Found: C, 67.17; H, 6.41.

Diels-Alder Reaction of 5 (R=OCH_3). To a solution of anhydrous aluminum chloride (0.88g) in nitrobenzene (25ml) was added **5b** (2g) and the resulting red solution was heated in a sealed tube at 85°C for 3

days. The resulting mixture consisted of a clear solution and starting material (0.5g, 25%). The solution was poured into ice-water and the mixture extracted with chloroform (4 x 25 ml). Evaporation of the organic solvent layer under vacuum gave **13** (1.2g, 60%), mp 273-275°C (acetone-ethanol). IR (KBr) 1610 (C=N), 1520, 1460, 1325 and 1180cm^{-1} (SO$_2$); NMR (CDCl$_3$-CF$_3$CO$_2$H) δ 7.9-6.7 (m, 16H, Ar*H*), 5.26-5.18 (d,

1H, =C*H*-ĊH-, 4.5-4.3 (m, 1H, =CH-Ċ*H*-), 4.24-4.1 (m, 1H), 3.96-3.84 (m, 1H), 3.74 (s, 3H, OCH$_3$), 3.68 (s, 3H, OCH$_3$); *m/z* (rel. intensity) 598 (M$^+$, 4), 534 (-SO$_2$, 21), 470 (-2SO$_2$, 50), 469 (-2SO$_2$, -H, 60), 455 (-2SO$_2$, -CH$_3$, 19), 368 (31), 367 (20), 366 (10), 299 (60), 298 (100). *Anal.* Calcd. for C$_{32}$H$_{26}$N$_2$O$_4$S$_2$: C, 64.21; H, 4.35. Found: C, 64.41; H, 4.33.

The addition of an excess of dimethyl acetylenedicarboxylate had no effect on the course of the reaction.

5a-Methyl-5,5a-dihydro-4-oxopyrido[1,2-*b*]-1,2-benzisothiazolin-1,1-dioxide (3; R=CH$_3$). A solution of 3-methyl-1,2-BID (0.5g, 2.7 mmole) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (0.48g, 2.7 mmole)^{24} in dry toluene under N$_2$ was boiled under reflux for 42 h. The cooled mixture was filtered from some unchanged starting BID, the solvent evaporated and the product purified by preparative TLC (SiO$_2$, CH$_2$Cl$_2$-petroleum ether 4:1 v/v to give **3** (R=CH$_3$) (0.31g, 45%), mp 164-166°C. IR (KBr) 1680 (C=O), 1600, 1330 and 1180cm$_{-1}$ (SO$_2$); NMR (CDCl$_3$): δ 8.0-7.4 (m, 5H, ArH + vinylic H), 5.6 (d, 1H, *J*=8Hz, vinylic H), 2.8 (s, 2H), 1.7 (s, 3H); *m/z* 249 (M$^+$). *Anal.* Calcd. for C$_{12}$H$_{11}$NO$_3$S: C, 57.81; H, 4.45. Found: C, 57.75; H, 4.51.

Reaction of Saccharin *Pseudo*chloride with Danishefsky's Diene. Saccharin *pseudo*chloride (0.52g, 2.6 mmole) was dissolved in dry toluene (20 ml) under N$_2$ and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (0.44g, 2.6 mmole) was added. The mixture was stirred at room temperature for 2 h. 4-Oxopyrido[1,2-*b*]-1,2-benzisothiazoline-1,1-dioxide (**14**) (0.45g, 75%) precipitated and was filtered. IR (KBr) 1650 (C=O), 1630, 1590, 1345, 1180cm^{-1}; NMR (CDCl$_3$) δ 8.45 (d, 1H, *J*=7Hz), 8.4-7.9 (m, 2H), 7.75-7.1 (m, 4H). Attempted recrystallization from ethanol led to hydrolysis to 2-(4-hydroxy-1*H*-2-pyridinium)benzenesulfonate (**15**), mp >300°C. IR (KBr) 3300-2200 (br), 1615, 1470, 1150cm^{-1}. *Anal.* Calcd. for C$_{11}$H$_9$NO$_4$S: C, 52.58; H, 3.61. Found, C. 52.41; H, 3.64.

***N*-Benzenesulfonyl-2,3-dihydro-2-phenyl-4-pyridone (16).** A solution of *N*-(benzenesulfonyl)phenylimine^{25} (0.8g, 3.3 mmole) and Danishevsky's diene (0.5g, 3.3 mmole) in dry toluene was boiled under a N$_2$ atmosphere under reflux for 4 h. The solvent was evaporated under vacuum and the residue dissolved in CH$_2$Cl$_2$ (20 ml). The extract was washed with 0.1 M HCl (5 ml), dried (MgSO$_4$) and evaporated. Flash chromatography of the residue (SiO$_2$, CH$_2$Cl$_2$-petroleum ether 9:1 v/v) gave **16** (0.85g, 80%), mp 145°C. IR (KBr) 1660 (C=O), 1595, 1365, 1290, 1160cm^{-1}. NMR (CDCl$_3$) δ 8.1-7.2 (m, 11H), 5.75-5.4 (m, 3H), 2.77-2.73 (m, 2H); *m/z* 313 (M$^+$). *Anal.* Calcd. for C$_{17}$H$_{15}$NO$_3$S: C, 65.17; H, 4.83. Found: C, 65.13; H, 4.89.

1,2,3,4-Tetrahydro-2-oxo-4-phenylpyrido[1,2-*b*]-1,2-benzisothiazoline-1,1-dioxide(17). 3-Methyl-1,2-BID (0.9g, 5 mmole) in dry THF was treated with cinnamoyl chloride (0.85g). Triethylamine (0.6g, 5 mmole) was added and the solution was boilded under reflux for 12 h. The solvent was evaporated and the residue chromatographed on a column of silica gel (benzene elution) to give **1 7**

(0.93g, 60%), mp 219°C (CH$_2$Cl$_2$/EtOH). IR (KBr) 1720 (C=O), 1320, 1160cm^{-1} (SO$_2$); NMR (DMSO-d$_6$) δ 8.3-7.5 (m, 4H), 7.2 (s, 5H), 6.8-6.5 (d, 1H, =CH), 4.4-3.9 (octet, 1H, ArCH-), 3.2-2.8 (m, 2H); m/z 311 (M$^+$)., 283 (-CO), 247 (-SO$_2$), 219 (-CO, -SO$_2$), 206 (-CO, -Ph). *Anal.* Calcd. for C$_{17}$H$_{13}$NO$_3$S: C, 65.59; H, 4.18. Found: C, 65.51; H, 4.24.

1,2-Dihydro-2-oxo-4-phenylpyrido[1,2-*b*]-1,2-benzisothiazoline-1,1-dioxide (18). **17** (0.31g, 1 mmole) and DDQ (0.23g, 1 mmole) were boiled under reflux in benzene (80 ml) for 3 h. A yellow solid precipitated on cooling and was filtered to give **18** (0.3g, quantitative), mp 280°C (CHCl$_3$/acetone). IR (KBr) 1660 (C=O), 1340, 1150cm^{-1} (SO$_2$); m/z 309, (M$^+$)., 281 (-CO), 245 (-SO$_2$, 217 (-CO, -SO$_2$). *Anal.* Calcd. for C$_{17}$H$_{11}$NO$_3$S: C, 66.02; H, 3.56. Found: C, 65.95; H, 3.63.

Reaction of Saccharin *Pseudo*chloride with 10. To a solution of saccharin *pseudo*chloride (2.015g) in dry acetonitrile (100 ml) was added a solution of **10** (1.11g) dropwise over 15 min with stirring at RT. After stirring for a further 12 h, evaporation of the solvent gave a thick red oil which was dissolved in EtOH and kept at 0°C for 12 h. The precipitated solid **19** (2.205g, 75%) had mp 122°C (abs. EtOH). IR (KBr) 1630 (C=O), 1330 and 1170 cm^{-1} (SO$_2$); NMR (CDCl$_3$) δ 8.1-7.6 (m, 4H, ArH), 4.5-4.2 (q, 1H, =C-CH-), 3.65-3.3 (q, 4H, N-CH$_2$), 1.85-1.65 (d, 3H, CH$_3$), 1.3-1.0 (m, 6, N-CH$_2$CH$_3$); m/z 294 (M$^+$).. *Anal.* Calcd. for C$_{14}$H$_{18}$N$_2$O$_3$S: C, 57.14; H, 6.12. Found, C, 57.03; H, 6.1. It was identical with the compound prepared (81%) from saccharin or from saccharin *pseudo*chloride and 2-lithio-*N,N*-diethylpropionamide at -78°C.

Reaction of 3-Ethoxy-1,2-BID with 10. A solution of 3-ethoxy-1,2-BID (2.21g) and **10** (1.11g) in acetonitrile was heated in a steel bomb at 180°C for 20 h. Evaporation of the solvent gave a black solid which, on recrystallization from ethanol, gave **20** as a yellow solid, mp 145°C (3.0g, 90%). IR (KBr) 1620 (C=N), 1300-1160cm^{-1} (SO$_2$); NMR (CDCl$_3$) δ 8.15-7.95 (m, 1H, ArH adjacent to SO$_2$), 7.6-7.3 (m, CH$_2$ 3H, ArH), 3.9-3.5 (q, 2H, -OCH$_2$), 3.5-3.0 (q. 4H, NCH$_2$), 2.8 (s, 3H, CH$_3$), 1.35-1.0 (m, 9H, OCH$_2$CH$_3$, NCH$_2$CH$_3$). *Anal.* Calcd for C$_{16}$H$_{22}$N$_2$O$_3$S: C, 59.62; H, 6.83. Found: C, 59.66; H, 6.91.

Hydrolysis of 20. **20** (1.61g) was heated under reflux with 85% H$_2$SO$_4$ (50 ml) for 20 h in an oil bath kept at 130°C. The mixture was then diluted with water (100ml), extracted with CHCl$_3$ (5x100 ml) and worked up as usual to give **21** (1.12g, 70%), mp 192°C (EtOH), which appeared to be a mixture of keto and enol forms in the solid state but not in solution in CDCl$_3$, where the keto form predominated. IR (KBr) 3500-3300 (O-H, bonded), 1700 (C=O), 1300 and 1150cm^{-1} (SO$_2$); NMR (CDCl$_3$) δ 7.9-7.3 (m, 4H, ArH), 3.8-3.3 (q, 1H, CO-H-), 3.3-2.7 (q, 4H, NCH$_2$), 2.0-1.7 (d, 2H, CH$_3$), 1.3-0.9 (t, 6H, NCH$_2$CH$_3$). *Anal.* Calcd. for C$_{14}$H$_{18}$N$_2$O$_3$S: C, 57.19; H, 6.17. Found: C, 57.03; H, 6.27.

Ring Expansion of 3-Trimethylsilyloxy-1,2-BID. Saccharin (3.66g) was dissolved in dry THF (40 ml) under N$_2$, and a solution of 1.73M butyllithium (11.60ml) in hexane was added dropwise to the solution cooled to -70°C. This was immediately followed by the addition of trimethylchlorosilane (2.54 ml) at the same temperature. The resulting clear solution was stirred at -60°C for 30 min and then at 0°C for 2 h (a white suspension formed at 0°C). Ynamine **10** (2.80 ml) was then added dropwise at 0°C and the mixture was stirred at 0°C for 2 h, at R.T. for 4 h, and finally boiled under reflux for 12 h. The mixture was poured into ice-water (100g) and the precipitate formed was filtered and dried (**2**; R=OSiMe$_3$), mp 152-153°C (Et$_2$O) (1.0g, 13.9%). The filtrate was extracted with ether (3x50 ml), the combined extracts were dried (MgSO$_4$)

and evaporated to give a thick yellow syrup. This was chromatographed on a short column of alumina and eluted with ethyl acetate to give **21** (1.53g, 26.7%), identical with material prepared as above. Compound **2** hydrolyzed quantitatively to **21** on standing at R.T. for 24 h. The structure of **2** (R=OSiMe$_3$) was confirmed by its physical properties: m/z 366 (M$^+$); NMR (CDCl$_3$) δ 8.2-7.3 (m, 4H, ArH), 4.0-3.0 (m, 4H, NCH_2), 2.1 (s, 3H, CH_3), 1.15 (t, 6H, NCH$_2$CH_3), 0.1 (s, 9H, SiCH_3). *Anal*. Calcd. for C$_{17}$H$_{26}$N$_2$O$_3$SSi: C, 55.71; H, 7.15. Found: C, 55.79; H, 7.19.

If the reaction was carried out at 0°C, *N*-methylsaccharin, (mp 126-127°, 4.1%) 5-*n*-butyl-3-diethylamino-4-methyl-1,2-benzothiazepine-1,1-dioxide, (**2**; R=Bu), mp 95.5-95.6°C (20.1%) and **21** (0.34%) were isolated, and were identical with authentic samples.

Reaction of Saccharin with 10.

a. 1 Equivalent of 10. Ynamine **10** (0.70 ml) was added dropwise to a solution of saccharin (0.91g) in dry acetonitrile (20ml) at 0°C and stirred at R.T. for 4 h. Evaporation of the solvent, and trituration of the residual orange gum with dry ether, filtration and evaporation of the ether gave **22** (1.12g, 76.2%), mp 105-106°C (Et$_2$O). IR (KBr) 1730 (C=O), 1340 and 1180cm^{-1} (SO$_2$); NMR(CDCl$_3$) δ 8.3-7.7 (m, 4H, ArH), 4.9 (q, 1H, J=7Hz, =CH), 3.1 (q, J=7Hz, 4H, NCH_2), 1.5 (d, J=7Hz, 3H, CH$_3$), 1.1 (t, J=7Hz, 6H, NCH$_2$CH_3); m/z 294 (M$^+$). *Anal*. Calcd. for C$_{14}$H$_{18}$N$_2$O$_3$S: C, 57.12; H, 6.16. Found: C, 57.09; H, 6.20.

b. 2 Equivalents of 10. Ynamine **10** (1.40 ml) was added to saccharin (1.83g) in dry acetonitrile (50 ml) as in *a* above. Another portion of ynamine (1.40 ml) was added to the yellow solution of **22** dropwise at room temperature and the solution was boiled under reflux for 48 h. The resulting cherry red solution was evaporated under reduced pressure to give a brown syrup which, on trituration with ethyl acetate (10ml), gave colorless crystals to which structure **24** is tentatively assigned; mp 117.5-118°C (1.17g, 28.9%). IR (KBr) 1640 (C=O, 1320 and 1150cm^{-1} (SO$_2$); ^{1}H NMR (CDCl$_3$) δ 7.9-7.4 (m, 4H, ArH), 4.0 (m, 1H, CH), 3.7-3.3 (dq, J=7Hz, 8H, NCH_2), 1.95 (d, J=2Hz, 3H, CH$_3$), 1.3 (t, 12H, NCH$_2$CH_3); ^{13}C NMR (CDCl$_3$) 169.6 (C=O), 167.7 (C=N), 145.6, 113.5, 131.2, 130.6, 122.9, 119.3, 101.0, 46.1, 43.9, 43.8, 16.0, 13.8, 10.5. *Anal*. Calcd. for C$_{21}$H$_{31}$NO$_3$S: C, 62.19; H, 7.70. Found: C, 62.06; H, 7.77. A similar product was obtained (27%) from 6-chlorosaccharin.[20b] Compound **24** was recovered unchanged on attempted hydrolysis, thus eliminating structure **23** from consideration.

3-(*N,N*-Diethylamino)-5-ethoxy-4-methyl-2-benzazepine-1-one (26, R=OEt).

3-Ethoxy-(1*H*)-1-isoindolone (**25**)[21] (0.585g) in dry THF (25 ml) under dry N$_2$ was treated with **10** (0.41g) and the mixture stirred for 3 days. It was filtered through Celite and the filtrate concentrated *in vacuo*. The product crystallized out and washed with cold ethyl acetate to give analytically pure **26** (R=OEt) (0.40g, 42%), mp 112-114°C. IR (KBr) 1640cm^{-1} (C=O); NMR(CDCl$_3$) δ 7.75 (m, 1H, H$_{10}$); 7.5 (m, 1H, H$_6$), 7.4 (m, 2H, H$_7$ & H$_8$), 3.8 (m, 2H, NCH_2), 3.3 (br m, 2H, O-CH_2), 2.1 (s, 3H, =C-CH_3), 1.2 (t, J=6Hz, NCH$_2$CH_3), 1.1 (br s, 3H, OCH$_2$CH_3); m/z (rel. intensity) 286 (M$^+$, 27), 258 (-CO, 18), 257 (-Et, 100), 241 (-OEt, 100), 186 (-NEt$_2$, -CO, 47). *Anal*. Calcd. for C$_{17}$H$_{22}$N$_2$O$_2$: C, 71.30; H, 7.74. Found: C, 71.30; H, 7.76.

3-(*N,N*-Diethylamino)-4-methyl-5-phenyl-2-benzazepine-1-one (26, R=Ph).

(*a*) 3-*n*-Butoxy-2,3-dihydro-3-phenyl-1-isoindolone[22] (1.0g) was heated under vacuum to its mp (oven temperature

140°C) in a Kugelrohr apparatus. After cooling to R.T. the vacuum was lowered to 0.02 mm/Hg and the oven heated to 230°C. A yellow oil distilled (0.74g) and was collected in the receiver bulb at 0°C. The oil was dissolved in dry acetonitrile (20 ml) under N_2 and **10** (0.5 ml) added. The solution was boiled under reflux for 18 h when TLC showed that no starting materials remained. Work up as usual gave a solid mixed with an oil which, or trituration with ether, gave **26** (R=Ph) (0.57g, 51%), mp 184.5-185°C (ethyl acetate/hexane). IR (KBr) 1630 (C=O), 1530cm⁻¹ (C=N); NMR (CDCl₃) δ 8.2-7.0 (m, 9H, Ar*H*), 4.05 (q, *J*=7Hz, 4H, NC*H₂*), 2.3 (s, 3H, =C-C*H₃*), 1.5 (t, *J*=7Hz, 6H, NCH₂C*H₃*); *m/z* (rel. intensity) 318 (M⁺, 23), 303 (-CH₃, 99), 246 (-NEt₂, 42), 241 (-Ph, 100). *Anal.* Calcd. for C₂₁H₂₂N₂O: C, 79.21; H, 6.96. Found: C, 79.21; H, 6.98.

(*b*) 2,3-Dihydro-3-hydroxy-3-phenyl-1-isoindolone (**28**) (1.125g) was suspended in dry acetonitrile (20ml) at 0°C under N_2 and treated with **10** (2.1 ml) dropwise at 0°C. The resulting clear yellow solution was stirred for 1 h at RT and then boiled under reflux for 20 h. The residue after evaporation of the solvent was triturated with ether to give **29**, mp 220-221°C (22.3%) (for characterization see next experiment). Evaporation of the ether gave a dark brown syrup which, on chromatography on a column of silica gel (ethyl acetate eluant), gave **26** (R=Ph) (8.8%), mp 186-187°C, identical (IR, NMR) with the compound prepared as under (*a*) above. Also isolated from the column was a yellow crystalline solid (0.26%), mp 277-279°C (EtOH), which cannot be assigned a structure at present owing to the small amount of material obtained; *m/z* 387 (M⁺). *Anal.* Calcd. for C₂₃H₂₁N₃O₃: C, 71.32; H, 5.43; N, 10.85. Found: C, 71.31; H, 5.53; N, 10.80.

Reaction of *N*-Trimethylsilylphthalimide with Phenyllithium and 10.

(a) A solution of phenyllithium [from bromobenzene (2.3 ml) and lithium (0.3g) in dry ether] was added dropwise to *N*-trimethylsilylphthalimide²⁶ (4.38g) in dry ether (100 ml) at 0°C under N_2. The white slurry was stirred at RT for 1 h and boiled under reflux for 48 h. Ynamine **10** (2.8 ml) was then added at 0°C and the mixture was then boiled for another 48 h. The mixture was poured into ice-water (100g) and extracted with ether (3x100 ml). The dried (MgSO₄) extracts were evaporated to give an orange syrup which was chromatographed on a silica gel column and eluted with ethyl acetate: petroleum ether (bp 40-60°C). The following products were eluted in the order shown:

27 (0.58g, 27.1%), mp 227°C (CH₃CO₂Et), yellow prisms. IR (KBr) 3180 (NH), 1780, 1720, 1685cm⁻¹ (C=O); ¹H NMR (CDCl₃) δ 9.0 (bs, 1H, N*H*, exchangeable with D₂O), 8.0-7.65 (m, 5H, Ar*H*), 7.5-7.1 (m, 8H, Ar*H*), 2.8-2.4 (m, 2H, NC*H₂*), 1.75 (s, 3H, C*H₃*-C=), 0.9 (t, *J*=7Hz, 6H, NCH₂C*H₃*); ¹³C NMR (CDCl₃) 169.4, 168.2, 167.2 (C=O), 150.6, 143.3, 135.4, 134.5, 133.5, 132.0, 131.4, 128.7, 128.3, 127.6, 126.0, 124.0, 123.7, 69.8 [Ar₂*C*(N)N], 46.7, 19.9, 13.2; *m/z* 465 (M⁺). *Anal.* Calcd. for C₂₉H₂₇N₃O₃: C, 74.82; H, 5.85. Found: C, 74.58; H. 5.88. **29** (0.17g, 2.5%), mp 220-221°C (ethyl acetate). IR (KBr) 33.60 (OH), 1690 (C=O), 1620cm⁻¹ (C=N); ¹H NMR (CDCl₃) δ 8.15 (s, 1H, OH, exchangeable), 7.9-7.1 (m, 9H, Ar*H*), 3.9 (q, *J*=7Hz, 1H, C*H*), 3.6-3.0 (m, 4H, NC*H₂*), 1.2 (d, *J*=7Hz, 3H, C*H₃*), 0.85-0.75 (2t, *J*=7Hz, 6H, NCH₂C*H₃*); ¹³C NMR (CDCl₃) 173.4 (C=O), 169.9 (N=*C*-Ar), 149.4, 142.1, 132.5, 131.7, 127.7, 127.4, 126.9, 124.1, 122.9, 121.0, 68.6 [Ph₂*C*(N)O], 42.85, 42.2, 39.9, 14.6, 12.7, 12.3; *m/z* 336 (M⁺). *Anal.* Calcd. for C₂₁H₂₄N₂O₂: C, 74.97; H, 7.19. Found, C, 75.05; H, 7.24. **30** (0.31g, 5.1%), mp 162-163°C (ether). IR (KBr) 3180 (br, OH, bonded), 1690 (C=O),

1630cm^{-1} (C=N); ^{1}H NMR (CDCl$_3$) δ 9.1 (s, 1H, OH), 8.4-7.2 (m, 9H, ArH), 4.0-3.5 (m, 5H, CH + NCH_2), 1.1 (m, 6H, CH_3 + NCH$_2$CH_3), 0.7 (t, J=7Hz, 3H, NCH$_2$CH_3); ^{13}C NMR (CDCl$_3$) 171.9 (C=O), 170.7 (C=N), 147.7, 140.9, 132.6, 131.5, 128.0, 127.7, 126.0, 124.5, 124.0, 120.9, 69.7 [Ar$_2$C(N)O], 43.0, 42.5, 40.3, 14.6, 14.3, 12.3; m/z 336 (M$^+$). Anal. Calcd. for C$_{12}$ H$_{24}$N$_2$O$_2$: C, 74.97; H, 7.19. Found: C, 75.05; H, 7.24. **26** (R=Ph) (0.52g, 8.2%), mp 186-187°C, identical with material obtained above. **28** (0.014g, 0.33%), mp 161.5-163°C, identical with an authentic sample. When the reaction was carried out in cold ether solution only **27** (14.6%), **29** (14.2%) and **30** (20.9%) were isolated.

(b) The above experiment was repeated but using dry THF as solvent and 2 equivalents of ynamine (5.60 ml). The solution was boiled as before and the cherry red solution worked up (vide supra). Column chromatography of the syrup on silica gel and elution with ethyl acetate/petroleum ether (2:1 v/v) gave a small amount of an unidentified compound which hydrolyzed to give phthalimide; this was followed by an orange solid, mp 277-279°C (EtOH). IR (KBr) 1710cm^{-1}; m/z 387, which could be **26** (R = N-phthalimido), and then by 3-diethylamino-1,2-dihydro-4-methyl-2-benzazepin-1,5-dione (**31**) (0.29g, 5.6%), mp 165.5-166°C (Et$_2$O). IR (KBr) 3200 (NH), 1720, 1690, 1680cm^{-1} (C=O); NMR (CDCl$_3$) δ 10.4 (s, 1H, NH), 8.0-7.4 (m, 4H,ArH), 3.8-3.2 (m, 4H, NCH_2), 2.3 (s, 3, CH_3), 1.35-1.1 (dt, 6H, NCH$_2$CH_3); m/z 258 (M$^+$). Anal. Calcd. for C$_{15}$H$_{18}$N$_2$O$_2$: C, 69.75; H, 7.02. Found: C, 69.64; H, 7.06.

Reaction of 2,3-Dihydro-3-hydroxy-3-phenylisoindol-1-one (28) with 10. Pure **28** (1.125g) was suspended in dry acetonitrile (20 ml) (N$_2$) at 0°C and treated with **10** (2.10 ml, 3 equiv.) and the resulting clear solution was stirred for 1 h at R.T. and boiled under reflux for 20 h. The syrup obtained after solvent evaporation was treated with ether to give **19** (0.29g, 20%). Chromatography of the extract on silica gel (EtOAc) gave **26** (0.14g, 8.8%), mp 186-187°C, identical with the sample obtained above.

Attempted Synthesis of 3-Diethylamino-1,2-dihydro-2,4-dimethyl-2-benzazepin-1,5-dione. To a stirred solution of 2-methyl-(1H)-isoindol-1,3(2H)-dione (N-methylphthalimide) (1.0g) in freshly distilled acetonitrile (30 ml) (N$_2$) was added **10** (0.86 ml). The mixture was heated under reflux for 12 h to give **32** (0.82g, 48%), mp 162-163°C. IR (KBr) 1705, 1680cm^{-1} (C=O); NMR (CDCl$_3$) δ 7.9-7.4 (m, 4H, ArH), 3.8-3.3 (m, 4H, NCH_2), 3.6 (s, 3H, NCH_3), 2.4 (s, 3H, C=C-CH_3), 1.3 (t, J=7Hz, 3H, NCH$_2$CH_3); m/z (rel. intensity) 272 (, 16), 200 (-NEt$_2$, 100), 173 (-NEt$_2$, -NMe, 76). Anal. Calcd. for C$_{16}$H$_{20}$N$_2$O$_2$: C, 70.56; H, 7.40. Found: C, 70.51; H, 7.42. Single crystal ORTEP diagrams are shown in Figs. 1 and 2. Lists of refined coordinates and esd's have been submitted by the Editor to the Cambridge Crystallographic Data Center. All measurements were made on a Nicolet R3mV diffractometer with graphite-monochromated MoKα radiation (λ = 0.71073Å). Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement of the setting angles at 20 carefully centered reflections in the range 15.26<2θ<26.30° corresponded to an orthorhombic cell with dimensions: a = 8.8199(28)Å, b = 13.02048(36)Å, c = 13.4771(40)Å, V=1457.5(8) Å^3. For Z=4 and F.W.272.38, the calculated density is 1.24g/cm^3. A total of 1500 reflections were collected.

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