The behaviour of the furazan-*N*-methanide analogue of the furoxan system. Ring expansion: new routes to 6*H*-1,2,5-oxadiazines. A combined experimental and theoretical study

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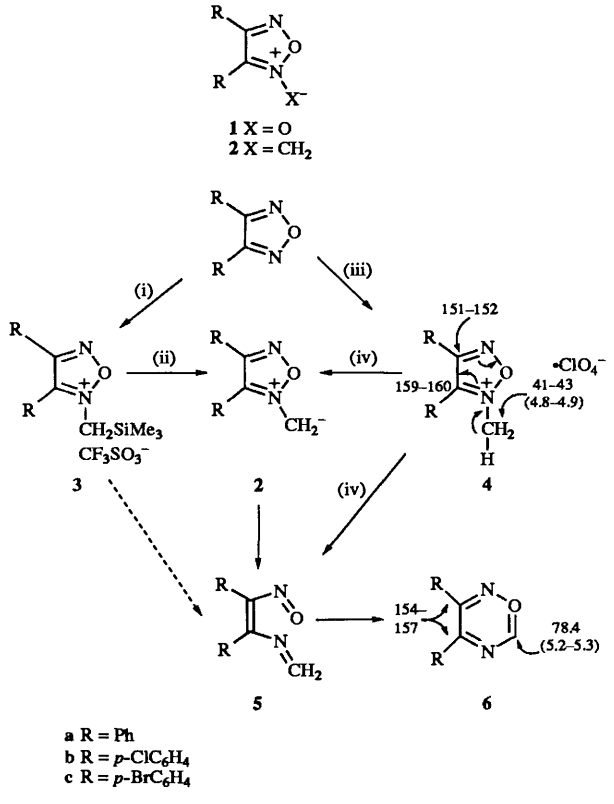
Desilylation of *N*-trimethylsilylmethyl- and deprotonation of *N*-methyl-1,2,5-oxadiazolium (furazan) salts gave ring expansions to 6*H*-1,2,5-oxadiazines; the results of 6-31G calculations on the expected furazan-*N*-methanide intermediate are reported.

Despite the long historical interest[1-3] in the furoxan system, **1**, so much so that this system has its own nomenclature[1] arising from early structural ambiguities, the carbon analogue, the furazan-*N*-methanide **2**, is unknown. Our interest in



Scheme 1 Some ^{13}C (and ^{1}H) NMR shift ranges shown. *Reagents:* i, trimethylsilylmethyl trifluoromethanesulfonate; ii, CsF; iii, dimethyl sulfate and sodium perchlorate; iv, lithium diisopropylamide or potassium *tert*-butoxide.

exocyclic azolium ylide 1,3-dipole systems led us to generate the first 1,2,3-triazolium-1-methanide species[4] by treating a *N*-trimethylsilylmethyl salt with caesium fluoride following a literature desilylation procedure.[5,6] Despite their low basicity it has now proved possible to obtain similar quaternised salts **3** of the furazan system and to desilylate them in a process which should likewise produce **2**, the furazan-*N*-methanide analogue of the furoxan system.

Table 1 Products

Compound (substrate)	Mp (*T*/°C)	Yield (%)	Compound	Mp (*T*/°C)	Yield (%)
3a	160–162[a]	52	**6a**	116–118	90[d]
3b	182–184[a]	51	**6b**	82–84	83[d]
4a	140–141[b]	90	**6a**	116–118	80,[e] 91[f]
4b	174–175[b]	88	**6b**	82–84	80,[e] 97[f]
4c	188–190[b]	91	**6c**	108–110	83,[e] 86[f]

[a] From dichloromethane–diethyl ether. [b] From acetone–diethyl ether. [c] From dichloromethane–hexane. [d] From the reaction of **3** with CsF. [e] From the reaction of **4** with lithium diisopropylamide. [f] From the reaction of **4** with potassium *tert*-butoxide.

The salts **3** were obtained by heating the parent furazans with trimethylsilylmethyl trifluoromethanesulfonate,[4] and the *N*-methyl salts **4** were obtained by using dimethyl sulfate followed by anion exchange with an excess of sodium perchlorate. The salts **3** were labile and gave loss of Me_3Si group on TLC plates or chromatographic columns and also in NMR solvents in which they began to ring-expand to the 1,2,5-oxadiazines **6**. Treatment with CsF[5,6] in dichloromethane at ambient temperatures gave high yields of the compounds **6** (Table 1). By analogy with our previous results on triazoles we propose that this desilylation produces the furazan methanide **2**. However, extensive attempts to trap this with the reactive electron-deficient dipolarophile dimethyl acetylenedicarboxylate[4] (which trapped the corresponding triazole-*N*-methanide) and the electron-rich dipolarophile 1-(pyrrolidin-1-yl)cyclohexene gave the products **6** even at temperatures down to −20 °C where the desilylation stopped. Hence, in contrast, to the furoxan structure **1**, the proposed furazan methanide structure **2** rapidly ring-opens to **5** thereby providing a new route to the oxadiazines **6** by electrocyclisation. Similar ring-opening occurs with the 1,2,3-triazolium-1-methanide system but, in this case, the ring N–N bond cleaves more slowly than the N–O bond of **2** allowing the methanide to be trapped.[4] The compounds **6** were also obtained by treatment of the *N*-methyl salts **4** with lithium diisopropylamide or potassium *tert*-butoxide (Table 1). This latter type of ring expansion was also observed[7] with the corresponding *N*-methyl-1,2,3-triazolium salts where it was found that the methanide intermediate analogous to **2**, which could have been trapped, was not present and the reaction was an E_2-type process similar to a Hofmann degradation. In the limit the desilylation process could also approach this concerted E_2 process or indeed the deprotonation could change to a two-step process giving **2** as the acidity of the

Table 2 Reaction energies (ΔE_R) and activation barriers ΔE_{act}/kcal mol^{-1} [a]

	2 ⟶ 5		5 ⟶ 6		2 ⟶ 6	
	Furazan	Triazole[c]	Furazan	Triazole[c]	Furazan	Triazole[c]
ΔE_R	−30.88	−26.10	−24.63	−25.62	−55.51	−51.72
ΔE_{act}	14.44	15.09	10.70	13.66	—	—
ΔG_R[b]	−32.77	−27.92	−20.82	−21.85	−53.59	−49.77
ΔG_{act}[b]	13.61	14.52	11.79	13.25	—	—

[a] 1 cal = 4.18 J. [b] ($\Delta G = \Delta H - 298.15\Delta S$). [c] Replace NH for O in Scheme 1.

CH increases with the increasing electron-withdrawing character of the ring. However, it has been well established[4–6] that desilylations of *N*-trimethylsilyl salts with CsF produce 1,3-dipoles containing the $=N^+-CH_2^-$ entity. Theoretical calculations using the 6-31G basis set from the Gaussian 92 series of programs[8] confirmed that the species **2** would rapidly ring-open. For these calculations the geometry optimisations were performed using analytical second derivatives and the proper number of eigen values verified. The results (Table 2) for the unsubstituted series (R = H) show a large gain in stability for the transformations **2** ⟶ **5** and **5** ⟶ **6** for both the furazan and triazole cases. The overall free-energy change for **2** ⟶ **6** is −53.6 kcal mol^{-1}. The activation barriers for each of the steps are low being < 15 kcal mol^{-1} but for the furazan case these activation barriers are 1–2 kcal mol^{-1} lower than for the triazole case. Since the methanide dipole was short lived and trapped only with difficulty in the triazole case, the replacement of the ring N–N bond by the N–O bond appears to have slipped the dipole over the threshold where it can be trapped for synthesis. Earlier work[9] before the recognition of electrocyclisations, shows that ring expansion to oxazines also occurs on deprotonation of *N*-methylisoxazolium salts and we have found that *N*-trimethylsilylmethyl salts of isoxazoles also desilylate with ring expansion suggesting a general process for heterocycles containing ring N–O bonds. The same process did not occur with *N*-methylpyrazolium salts, the nitrogen analogues of the isoxazole system.[10]

Experimental

The furazan substrates were prepared by literature[1–3] procedures. The products **3**, **4** and **6** were obtained by the following typical methods.

(i) 3,4-Diphenyl-2-trimethylsilylmethyl-1,2,5-oxadiazol-2-ium trifluoromethanesulfonate 3a

A suspension of 3,4-diphenylfurazan (1.0 g, 4.5 mmol) in trimethylsilylmethyl trifluoromethanesulfonate (1.8 cm^3, 9.0 mmol) was stirred at ambient temperature for 24 h and then treated with diethyl ether (100 cm^3) whereupon the title compound **3a** separated (1.5 g, 52%), mp 160–162 °C (from dichloromethane–diethyl ether) (Found: C, 49.4; H, 4.4; N, 6.3. $C_{19}H_{21}F_3N_2O_4SSi$ requires C, 49.8; H, 4.6; N, 6.1%); $\delta_H(CD_2Cl_2)$ 5.63 (s, 2 H, NCH_2) and 7.36–7.69 (m, 10 H, Ph). The only other material encountered was recovered furazan.

(ii) 2-Methyl-3,4-diphenyl-1,2,5-oxadiazol-2-ium perchlorate 4a

A solution of 3,4-diphenylfurazan (1.0 g, 4.5 mmol) in dimethyl sulfate (5 cm^3) was stirred at 80 °C for 48 h, cooled, treated with aqueous sodium perchlorate (0.7 g, 10 cm^3), stirred and then treated with diethyl ether (50 cm^3) to give the title compound **4a** (1.36 g, 90%), mp 140–141 °C (from acetone–diethyl ether) (Found: C, 53.3; H, 3.9; N, 8.2. $C_{15}H_{13}ClN_2O_5$ requires C, 53.5; H, 3.9; N, 8.3%); δ_H([$^2H_6$]acetone) 4.9 (s, 3 H, NMe) and 7.76–8.03 (m, 10 H, Ph); δ_C 41.7 (NMe), 152.0 (C-4), 160.0 (C-3), 120.2, 130.3, 130.9 and 133.7 (C-3, phenyl, C-1′, C-2′, C-3′, C-4′, respectively) and 123.0, 130.5, 131.5 and 135.3 (C-4, phenyl, C-1′, C-2′, C-3′, C-4′, respectively).

(iii) 3,4-Diphenyl-6*H*-1,2,5-oxadiazine 6a

(*a*) A solution of **3a** (470 mg, 1.02 mmol) in dichloromethane (10 cm^3) was treated with caesium fluoride (300 mg, 2 mmol), stirred at ambient temperature for 24 h, filtered to remove salts, and then evaporated under reduced pressure. The residue (crude **6a**) in dichloromethane (5 cm^3) was placed on a column of silica gel 60 (Merck 230–400 mesh ASTM) and pure **6a** (230 mg, 90%) was eluted with dichloromethane–ethyl acetate (95 : 5, v/v), mp 116–118 °C (from dichloromethane–hexane) (Found: C, 76.15; H, 5.2; N, 11.6. $C_{15}H_{12}N_2O$ requires C, 76.25; H, 5.1; N, 11.9%); $\delta_H(CDCl_3)$ 5.28 (s, 2 H, NCH_2O) and 7.1–7.3 (m, 10 H, two Ph); δ_c 78.3 (CH_2), 157.4, 156.25 (C-3, C-4), 135.1, 128.3, 128.5 and 130.4 (C-3 Ph, C-1′, C-2′, C-3′, C-4′, respectively) and 132.1, 127.9, 128.3 and 130.1 (C-4 Ph, C-1′, C-2′, C-3′, C-4′, respectively).

(*b*) A solution of **4a** (1.0 g, 2.97 mmol) in toluene (30 cm^3) was treated with potassium *tert*-butoxide (0.4 g, 3.56 mol) and the mixture stirred at ambient temperature for 20 h, filtered and evaporated to give a residue of crude compound **6a** which was purified as described above (yield from column, 91%).

(*c*) A solution of lithium diisopropylamide prepared from Li metal (23 mg, 3.26 mmol), diisopropylamine (360 mg, 3.6 mmol) dry tetrahydrofuran (2.16 g) and isoprene (120 mg) with sonication, was treated with a solution of **4a** (1.0 g, 2.97 mmol) in tetrahydrofuran (10 cm^3), stirred at ambient temperature for 5 min and then worked-up as described above to give compound **6a** (80%).

References

1 R. M. Paton, in *Comprehensive Heterocyclic Chemistry*, series eds. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 6, ed. K. T. Potts, pp. 393–426.
2 A. Albini and S. Pietra, in *Heterocyclic N-Oxides*, CRC Press Inc., Boca Raton, Florida, 1991, pp. 58–60; 81–83, 187.
3 C. Grundmann and P. Grunanger, *The Nitrile Oxides*, Springer-Verlag, Berlin, 1971.
4 R. N. Butler, P. D. McDonald, P. McArdle and D. Cunningham, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1653.
5 E. Vedejs, S. Larsen and F. G. West, *J. Org. Chem.*, 1985, **50**, 2170.
6 R. C. F. Jones, J. R. Nichols and M. T. Cox, *Tetrahedron Lett.*, 1990, **31**, 2333.
7 R. N. Butler, J. P. Duffy, D. Cunningham, P. McArdle and L. A. Burke, *J. Chem. Soc., Perkin Trans. 1*, 1992, 147.
8 Gaussian 92, revision A. M. J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 1992.
9 E. P. Kohler and A. H. Blatt, *J. Am. Chem. Soc.*, 1928, **50**, 1217; E. P. Kohler and N. K. Richtmyer, *J. Am. Chem. Soc.*, 1928, **50**, 3092; E. P. Kohler and W. F. Bruce, *J. Am. Chem. Soc.*, 1931, **53**, 644; J. F. King and T. Durst, *Can. J. Chem.*, 1962, **40**, 882.
10 R. N. Butler, H. A. Gavin, D. Cunningham and P. McArdle, *J. Chem. Res.*, 1994, (*S*), 12.

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