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The bromination and nitration of some (2*H*)-1, 4-benzoxazin-3(4*H*)-ones

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Conditions are described for the bromination and nitration of (2*H*)-1,4-benzoxazin-3(4*H*)-3-one, its 6-chloro and 6-methyl analogues and (2*H*)-1,4,-benzothiazin-3(4*H*)-one at C–6 and C–7 and for the dibromination (6, 7–) and dinitration (6, 8–) of (2*H*)-1,4-benzoxazin-3(4*H*)-3-one.

Keywords: (2*H*)-1,4-benzoxazin-3(4*H*)-ones, bromination, nitration

The (2*H*)-1,4-benzoxazin-3(4*H*)-one ring system is present in a number of biologically active natural products including the phytoalexins of grasses, which are formed *in vitro* by the hydroxylation of (2*H*)-1,4-benzoxazin-3(4*H*)-one.[1] In connection with the preparation of potential anti-fungal agents modelled on these compounds, we had occasion to examine the aromatic substitution of some (2*H*)-1,4-benzoxazin-3(4*H*)-ones.[2] Prior work on the aromatic substitution of (2*H*)-1,4-benzoxazin-3(4*H*)-one has shown that monobromination gave firstly the 6-bromo and then the 6,7-dibromo derivative.[3] In contrast to this, nitration has been reported[4,5] to give the 6-nitro and then the 6,8-dinitro compound. Nitration of the 6-chloro compound gave the 6-chloro-7-nitro-1,4-(2*H*)-benzoxazin-3(4*H*)-one.[6] We have confirmed the orientation of these substitutions by nuclear Overhauser effect (nOe) enhancements based on irradiation of the N–H signal. This led to the identification of the H-5 signal. We have then extended the study of the aromatic substitution under different conditions in the context of preparing polysubstituted derivatives.

Bromination of (2*H*)-1,4-benzoxazin-3(4*H*)-one[7] (**4**, Scheme 1) with bromine in glacial acetic acid gave firstly the 6-bromo 3 and then the 6,7-dibromo compound **1** whilst bromine in chloroform gave mainly the 7-bromo derivative **6**. Bromination of the 6-chloro- and 6-methyl-(2*H*)-1,4-benzoxazin-3(4*H*)-ones and (2*H*)-1,4-benzothiazin-3(4*H*)-ones gave the 7-bromo compounds. Nitration of (2*H*)-1,4-benzoxazin-3(4*H*)-one **4** with a sulfuric acid:nitric acid mixture gave the 6-nitro **5** and then the 6,8-dinitro compound **2** whilst nitrosation : nitration with sodium nitrite:fuming nitric acid gave mainly the 7-nitro compound **7**. 6-Chloro-(2*H*)-1,4-benzoxazin-3(4*H*)-one gave the 7-nitro compound.

The orientation of bromination of these (2*H*)-benzoxazin-3 (4*H*)-ones parallels that of the substitution reactions of *N*-acetyl-*o*-anisidine including dibromination which gives 4, 5-dibromo-2-methoxyacetanilide.[9] However, dinitration gives 4,5-dinitro-2-methoxyacetanilide[10] and the 4,6-dinitro compound is only obtained on further nitration of 4-nitro-2-methoxy-*N*-toluene-*p*-sulfonylaniline.[11]

Techniques used: NMR spectroscopy, nOe enhancements

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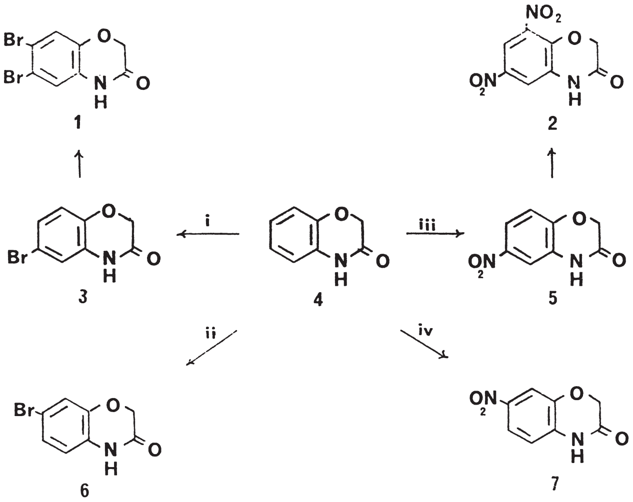

Scheme 1 *Reagents*:- (i) Br_2, glacial CH_3CO_2H; (ii) Br_2,$CHCl_3$; (iii) HNO_3, H_2SO_4; (iv) $NaNO_2$, HNO_3.

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References cited in this synopsis

1 E. Glawischnig, S. Grun, M. Frey and A. Gierl. *Phytochemistry*, 1990, **50**, 925.
2 See M. Sainsbury in *Rodd's Chemistry of Carbon Compounds*, Elsevier, Amsterdam, 2nd edn. 1978, vol. IV part H, chap.41 p.462.
3 M. Mazharuddin and G. Thyagarajan, *Ind. J. Chem.*, 1969, **7**, 658 (*Chem. Abs.*, 1969, **71**, 70552)
4 G. Newberry and M.A. Phillips, *J. Chem. Soc.*, 1928 3046.
5 J.E. Balaban, *J. Chem. Soc.*, 1929, 2607.
6 C.V. Reddy Sastry, K. Srinivasa Rao, V.S.H. Krishnan, K.Rastogi, M.L. Jain and G.K.A.S. Narayan, *Ind. J. Chem., Sect. B*, 1989, **28B**, 48 (*Chem. Abs.*, 1989, **111**, 174066).
7 X. Huang and C.C. Chan, *Synthesis*, 1984, 851.
9 M. Kohn, *J. Org. Chem.*, 1953, **18**, 530.
10 R. Meldola and J.V. Eyre, *J. Chem. Soc.*, 1902, **79**, 1076.
11 F. Bell, *J. Chem. Soc.*, 1960, 769.

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