A Novel Ring Expansion observed during the Intramolecular Cyclisation with *N*-Methoxy-*N*-acylnitrenium Ions generated from *N*-Methoxyamides: an Expedient Synthesis of 1,5-Benzodiazonine Derivatives

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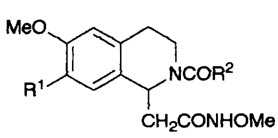
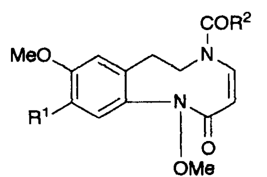
Cyclisation of *N*-methoxy-*N*-acylnitrenium ions generated from *N*-methoxyamides of 6-methoxy-1,2,3,4-tetrahydroisoquinoline-1-acetic acids with a hypervalent iodine compound proceeds through a spirocyclic intermediate followed by ring expansion to form 1,5-benzodiazonine derivatives in good yield.

Cyclisations *via* spirocyclic intermediates have been of interest both in synthesis and for mechanistic problems.[1] Although the spirocyclisation was sometimes unexpected, this process could lead to unusual compounds which would otherwise not be readily accessible, or provide an efficient synthesis of known compounds. For example, the transformation of benzylaminonitriles to cyclohepta[*c*]pyrrol-6(2*H*)-ones[2] and the oxidative ring expansion of isoquinoline enamides to 3-benzazepines[3] have recently been reported. In the application of cyclisation with an *N*-methoxy-*N*-acylnitrenium ion[4] to the synthesis of the natural alkaloid aaptamine,[5] we tried to cyclise compounds of type **1**. The reaction took an unexpected course and led to a new, preparatively useful synthesis of nine-membered benzofused azaheterocycles.

Thus, heating a solution of the *N*-methoxyamide **1a** (1 mmol) in $CHCl_3$ (15 ml) with $PhI(OCOCF_3)_2$ (1.3 mmol) at 65 °C for 3 min[4d] gave rise to the 1,5-benzodiazonine **2a**, m.p. 140–142 °C, in 62% yield. Compound **3** was not isolated. The structure of **2a** was determined from spectral and analytical data.† Measurement of ^1H–^1H 2D NMR nuclear Overhauser enhancements (NOEs) supported the structure; the correlations observed are shown in Fig. 1. Catalytic hydrogenation of **2a** gave **4a**, m.p. 213–214 °C (yield 33%) and **4b**, m.p. 55–57 °C (yield 54%). The *N*-methoxyamides **1b** and **c** underwent similar ring expansion reactions with $PhI(OCOCF_3)_2$ to give **2b**, m.p. 176–178 °C (yield 55%) and **2c**, oil (yield 76%), respectively.‡

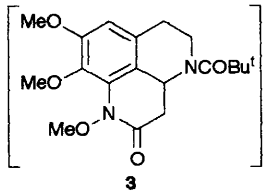


1



2

a; R^1 = OMe, R^2 = Bu^t
b; R^1 = OMe, R^2 = Me
c; R^1 = H, R^2 = Bu^t



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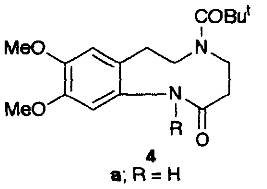

4
a; R = H
b; R = OMe

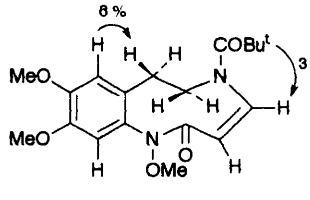

Fig. 1 NOEs for **2a**

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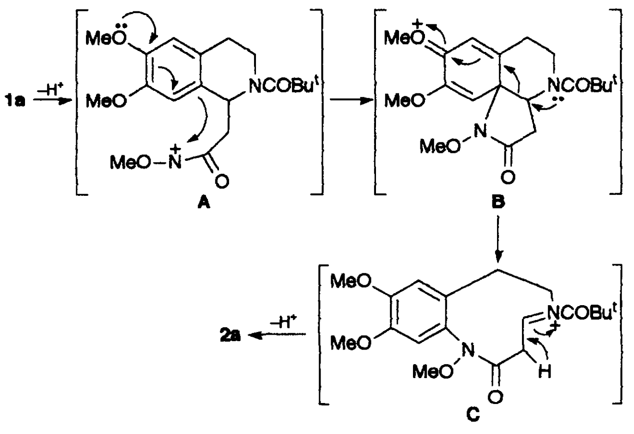
† For **2a**: ^1H NMR ($CDCl_3$): δ 1.01 (s, 9H), 3.08 (ddd, *J* 8.9, 10.8, 13.8 Hz, 1H), 3.28 (dd, *J* 7.4, 13.8 Hz, 1H), 3.55 (ddd, *J* 7.4, 10.8, 13.8 Hz, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 4.30 (dd, *J* 8.9, 13.8 Hz, 1H), 4.85 (d, *J* 10.3 Hz, 1H), 6.64 (s, 1H), 6.69 (s, 1H) and 6.70 (d, *J* 10.3 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 28.13 (q), 29.65 (t), 39.42 (s), 45.99 (t), 56.13 (q), 56.42 (q), 61.44 (q), 100.57 (d), 112.67 (d), 114.12 (d), 130.31 (s), 130.94 (s), 134.18 (d), 148.08 (s), 149.95 (s), 164.33 (s), 176.46 (s).

‡ New compounds were fully characterised by elemental analysis, NMR, IR and mass spectroscopy.



Scheme 1

The ring expansion may proceed *via* a mechanism involving spirocyclisation of the *N*-methoxy-*N*-acylnitrenium ion **A** to form intermediate **B** (Scheme 1). Fission of the ring junction of **B** would then result in ring expansion to afford the intermediate **C**; a similar type of ring cleavage has been postulated in the ring expansion of isoquinoline enamides.[3]

As only a limited number of synthetic methods for these ring systems have been reported,[6] the new synthesis of the 1,5-benzodiazonines appears to be useful and convenient in terms of the ready accessibility of the starting materials§ and operational simplicity.

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§ The *N*-methoxyamides **1** were synthesized by *N*-acylation followed by condensation with methoxyamine[4b] of 1,2,3,4-tetrahydroisoquinoline-1-acetic acids, which were conveniently prepared by the reported procedure.[7]