OXIDATION OF N^6-BENZYLADENINE WITH *m*-CHLOROPEROXYBENZOIC ACID: FORMATION OF THE N(1)-OXIDE†

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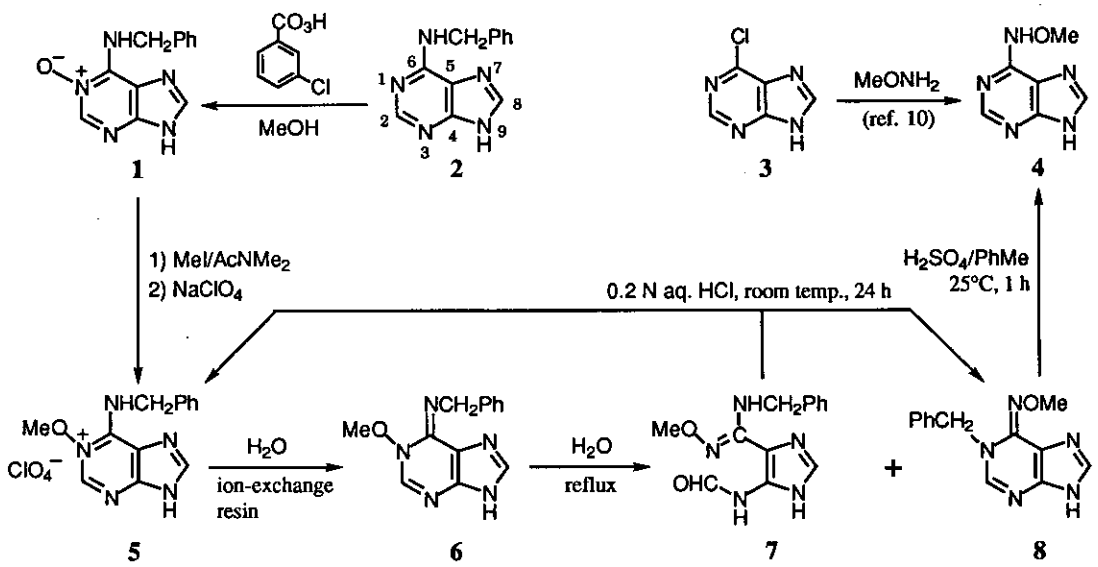
Abstract——Oxidation of N^6-benzyladenine (**2**) with *m*-chloroperoxybenzoic acid in MeOH has been found to give N^6-benzyladenine 1-oxide (**1**) as the main product. The structure of **1** has been established by leading it to N^6-methoxyadenine (**4**) through *O*-methylation, Dimroth rearrangement, and nonreductive debenzylation.

In 1982, Nasyr *et al.*[1] reported the preparation of an *N*-oxide [mp 222–224°C (decomp.)] of the synthetic cytokinin N^6-benzyladenine (**2**) in 33% yield by treating **2** with 15% aqueous H_2O_2 in trifluoroacetic acid at 65–70°C for 1 h or at 20°C for 17 h. The *N*-oxide was found to exhibit a cytokinin activity similar to that of **2** or kinetin,[1,2] but its chemical and spectral characterization was too incomplete to specify the location of the *N*-oxide function. In the present study, we investigated the *m*-chloroperoxybenzoic acid (MCPBA) oxidation of **2** in MeOH.

Treatment of **2** with MCPBA in MeOH at 30°C for 20 h furnished an *N*-oxide (mp 201–202°C)[3,4] in 35% yield, together with 25% recovery of **2**. The following chemical evidence permitted us to assign the 1-oxide structure (**1**) to this *N*-oxide (Scheme 1). On methylation with MeI in $AcNMe_2$ at 25°C for 20 h, **1** gave, after treatment of the product with aqueous $NaClO_4$, the 1-methoxy derivative as the perchlorate salt (**5**) [mp 195–197°C (decomp.)][5] in 72% yield. Conversion of **5** into the free base (**6**) by the use of Amberlite IRA-402 (HCO_3^-) and treatment of **6** with boiling H_2O for 18 h produced the oily monocyclic amidine derivative (**7**)[6] and the Dimroth

† Dedicated to Professor Alan R. Katritzky (University of Florida) on the occasion of his 65th birthday.

rearrangement product (**8**) [mp 241–242°C (decomp.)][7] in 16% and 56% yields, respectively. The monocycle (**7**) underwent recyclization in 0.2 N aqueous HCl at room temperature in 24 h, affording both the N^6-methoxy derivative (**8**) and the 1-methoxy isomer [isolated as the perchlorate salt (**5**)] in 63% and 15% yields, respectively. All these findings were analogous to those reported previously by us for N^6,9-dimethyladenine 1-oxide[8] and for adenine 1-oxide.[9,10]



Scheme 1

Final identification of **8** as the N^6-methoxy derivative rested on its nonreductive debenzylation leading to the formation of N^6-methoxyadenine (**4**). When debenzylated with conc. H_2SO_4 at 25°C for 1 h in the presence of toluene,[11] **8** provided **4** [mp *ca.* 200°C (decomp.)] in 87% yield, and this sample was identical with authentic **4**[10] synthesized from 6-chloropurine (**3**) and methoxyamine.

The uv spectra of **1** in H_2O at various pH's[4] corresponded to those[9,12] of adenine 1-oxide with an expected bathochromic shift of maxima due to N^6-benzylation. This suggests the preponderance of the N(1)-oxide form over the tautomeric N(1)-OH form in H_2O for the neutral species of **1**, as in the case of adenine 1-oxide.[13,14]

In summary, the above results reveal that the main product from the MCPBA oxidation of N^6-benzyladenine (**2**) is the 1-oxide (**1**). This directivity in oxidation is in general agreement with that observed in similar MCPBA oxidations of 9-substituted analogues, such as N^6,9-dimethyladenine,[8] N^6-methyladenosine,[15] and 2',3',5'-tri-*O*-benzoyl-N^6-methyladenosine.[15] Interestingly, a pilot experiment has suggested that the main product obtained

in our hands from the trifluoroperoxyacetic acid oxidation of **2** according to the procedure of the Russian group[1] is not **1**, but may be the N(7)-oxide. We are now in the process of confirming its outcome.

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3. Satisfactory analytical and/or spectroscopic data were obtained for all new compounds described.
4. Selected spectral data: ms *m/z*: 241 (M^+); uv $\lambda_{max}^{95\%\ aq.\ EtOH}$ 238 nm (ε 41800), 274 (11100); $\lambda_{max}^{H_2O}$ (pH 1) 265 (15200); $\lambda_{max}^{H_2O}$ (pH 7) 236 (39300), 273 (12200); $\lambda_{max}^{H_2O}$ (pH 13) 239 (47300), 279 (11200); ^{1}H nmr (Me_2SO-d_6) δ: 5.24 (2H, d, *J* = 6 Hz, NHC*H*$_2$Ph), 7.2–7.5 (5H, m, NHCH$_2$*Ph*), 8.28 [1H, s, C(8)-H], 8.58 [1H, s, C(2)-H], 8.84 (1H, t, *J* = 6 Hz, N*H*CH$_2$Ph), 13.42 [1H, broad (br), N(9)-H].
5. Selected spectral data for **5**: uv $\lambda_{max}^{95\%\ aq.\ EtOH}$ 269 nm (ε 13700); $\lambda_{max}^{H_2O}$ (pH 1) 264 (14800); $\lambda_{max}^{H_2O}$ (pH 7) 226 (shoulder) (18300), 277 (14500); $\lambda_{max}^{H_2O}$ (pH 13) 273 (16300); ^{1}H nmr (Me_2SO-d_6) δ: 4.19 (3H, s, OMe), 5.44 (2H, s, NHC*H*$_2$Ph), 7.2–7.5 (5H, m, NHCH$_2$*Ph*), 8.53 [1H, s, C(8)-H], 9.16 [1H, s, C(2)-H], 10.30 and 14.29 (1H each, br, two NH's).
6. Selected spectral data for **7**: ms *m/z*: 273 (M^+); ir $\nu_{max}^{CHCl_3}$ (at 0.005 M) 1670 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 3.79 (3H, s, OMe), 4.95 (2H, d, *J* = 7 Hz, NHC*H*$_2$Ph), 5.69 (1H, t, *J* = 7 Hz, N*H*CH$_2$Ph), 7.2–7.4 [6H, m, NHCH$_2$*Ph* and C(2)-H], 8.33 (1H, s, NHC*H*O), 10.04 and 11.12 (1H each, br, two NH's).
7. Selected spectral data for **8**: uv $\lambda_{max}^{95\%\ aq.\ EtOH}$ 276 nm (ε 10900); $\lambda_{max}^{H_2O}$ (pH 1) 280 (9100); $\lambda_{max}^{H_2O}$ (pH 7) 274 (11700); $\lambda_{max}^{H_2O}$ (pH 13) 277 (13800); ^{1}H nmr (Me_2SO-d_6) δ: 3.68 (3H, s, OMe), 4.98 (2H, s, C*H*$_2$Ph), 7.2–7.4 (5H, m, CH$_2$*Ph*), 7.88 [1H, d, *J* = 0.7 Hz, C(8)-H], 8.00 [1H, s, C(2)-H], 12.48 (1H, br, NH).
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