

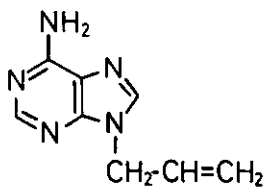
SYNTHESES OF 9-ALLYLADENINE 1-OXIDE AND 9-( $\Delta^2$ -ISOPENTENYL)ADENINE  
1-OXIDE

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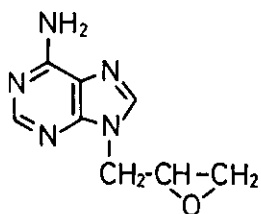
**Abstract**—An unequivocal synthesis of 9-allyladenine 1-oxide (III) has been accomplished by an initial alkylation of 1-ethoxyadenine (VI) with allyl bromide and the Et—O bond cleavage of the resulting 9-allyl-1-ethoxyadenine hydrobromide (VII) with pyridine. 9-( $\Delta^2$ -Isopentenyl)adenine 1-oxide (IX) was also prepared in a similar manner.

Oxidation of 9-allyladenine (I) with perbenzoic acid was reported by Kondo *et al.*<sup>1</sup> to give 9-(2,3-epoxypropyl)adenine (II) in 63% yield, although the uv spectrum of the oxidized material was suggestive of the 1-N-oxide structure (III). The recent communication by DiMenna and Piantadosi<sup>2</sup> reported that a similar oxidation of I with *m*-chloroperbenzoic acid produced 9-allyladenine 1-oxide (III) and not the epoxypropyl derivative II as claimed by the Japanese workers. However, the evidence adduced by the American group for assignment of the 1-N-oxide structure also seemed somewhat inconclusive. This prompted us to prepare the N-oxide III through an unambiguous synthetic route that should not include a step to expose the allylic side chain to oxidation.

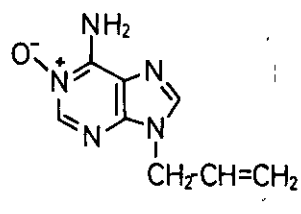
The starting material selected in the present synthesis was 1-ethoxyadenine (VI),<sup>3</sup> which was easily obtainable by the peracetic acid oxidation of adenine (IV)<sup>3,4</sup> followed by ethylation of the resulting 1-N-oxide V.<sup>3</sup> Treatment of VI with allyl bromide in AcNMe<sub>2</sub> at room temperature (26–32°C) for 48 h furnished the allylated product VII [mp 204–208°C (dec.);  $\lambda_{\max}^{95\% \text{ EtOH}}$  259 nm ( $\epsilon$  12700);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 1) 260 (12900);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 7) 260 (12800);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 13)<sup>5</sup> 258 (13400), 265 (sh) (12000)]<sup>6</sup> in 67% yield. The assignment of the 9-substituted structure was based on the generalization that 1-alkoxyadenines undergo alkylation mainly at the 9-position<sup>3</sup> and on the uv spectra



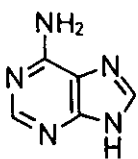
I



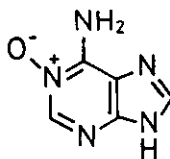
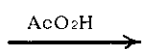
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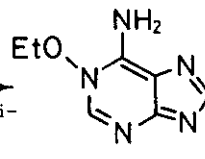
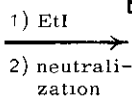
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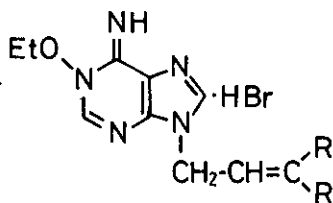
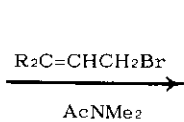
IV



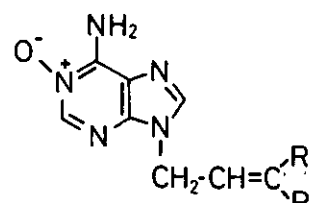
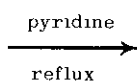
V



VI



VII, R = H  
VIII, R = Me



III, R = H  
IX, R = Me

similar to those<sup>3,7</sup> of 1-alkoxy-9-alkyladenines. Removal of the ethyl group from VII was then effected with boiling pyridine (1 h) to give the desired N-oxide III [mp 265–269°C (dec.)] in 86% yield. The easy cleavage of the Et–O linkage was in general agreement with the facile dealkylation<sup>8,9</sup> of 1-alkoxy-9-alkyladenine salts on nucleophilic attack. The structure of III was supported by similarity of its uv spectra [ $\lambda_{\max}^{95\% \text{ EtOH}}$  235 nm ( $\epsilon$  42300), 263 (8000), 300 (2100);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 1) 259 (12300);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 7) 232 (45300), 262 (8100), 292 (2100);  $\lambda_{\max}^{\text{H}_2\text{O}}$  (pH 13) 232 (28500), 269 (8700), 305 (4100)] to those<sup>7</sup> of 9-alkyladenine 1-oxides and by its nmr spectrum [(CF<sub>3</sub>CO<sub>2</sub>D)  $\delta$ : 5.16 (2H, d,  $\underline{J}$  = 6 Hz, NCH<sub>2</sub>CH), 5.62 (1H, d,  $\underline{J}$  = 17.5 Hz, trans CH=CH<sub>2</sub>), 5.66 (1H, d,  $\underline{J}$  = 9 Hz, cis CH=CH<sub>2</sub>), 5.80–6.32 (1H, m, CH<sub>2</sub>CH=CH<sub>2</sub>), 8.92 and 9.17 (1H each, s, purine protons)] indicating that the allylic side chain was kept intact.

The synthetic generality of the above scheme was then checked by a parallel synthesis of 9-( $\Delta^2$ -isopentenyl)adenine 1-oxide (IX), the 1-N-oxide of one of the positional isomers of triacanthine.<sup>10</sup> Alkylation of VI with 3-methyl-2-butenyl bromide (AcNMe<sub>2</sub>, 29–33°C, 12 h) produced the salt VIII [mp 207.5–210.5°C (dec.)] in 66% yield. On treatment with boiling pyridine for 1 h, VIII afforded the N-oxide IX [88% yield; mp 266.5–268.5°C (dec.); nmr (CF<sub>3</sub>CO<sub>2</sub>D)  $\delta$ : 1.96 (6H, s, CMe<sub>2</sub>), 5.15 (2H, d,  $\underline{J}$  = 8 Hz, NCH<sub>2</sub>CH), 5.59 (1H, t,  $\underline{J}$  = 8 Hz, CH<sub>2</sub>CH=C), 8.94 and 9.24 (1H each, s, purine protons)]. The uv spectra of VIII and IX matched those of VII and III, respectively.

Thus, the present results have demonstrated the synthetic utility of the 1-ethoxy group for preparation of adenine 1-oxide derivatives possessing unsaturated side chains at the 9-position.

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