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DNA Apurinic Sites: Synthesis of a Model Compound and Study of its Reactivity with 3-Aminocarbazole

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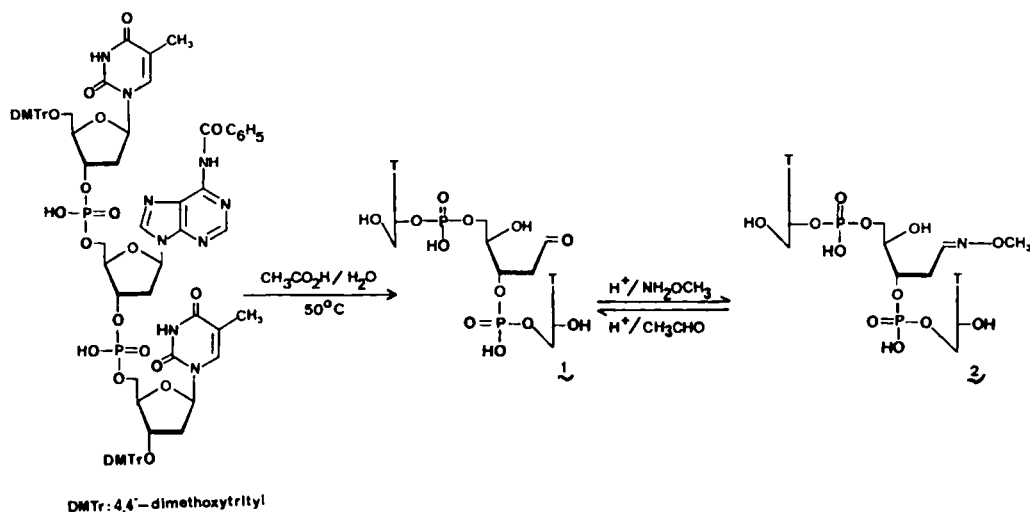
DNA APURINIC SITES : SYNTHESIS OF A MODEL COMPOUND
AND STUDY OF ITS REACTIVITY WITH 3-AMINOCARBAZOLE

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Summary The mechanism of breakage of apurinic DNA with 3-aminocarbazole was determined on a short oligonucleotide model. The results founded contrast with those reported in the literature.¹

Using the phosphotriester approach in solution the fully-protected trinucleotide diphosphate TpApT was synthesized. Subsequent phosphate deprotection and careful acidic treatment which removed the trityl protec-

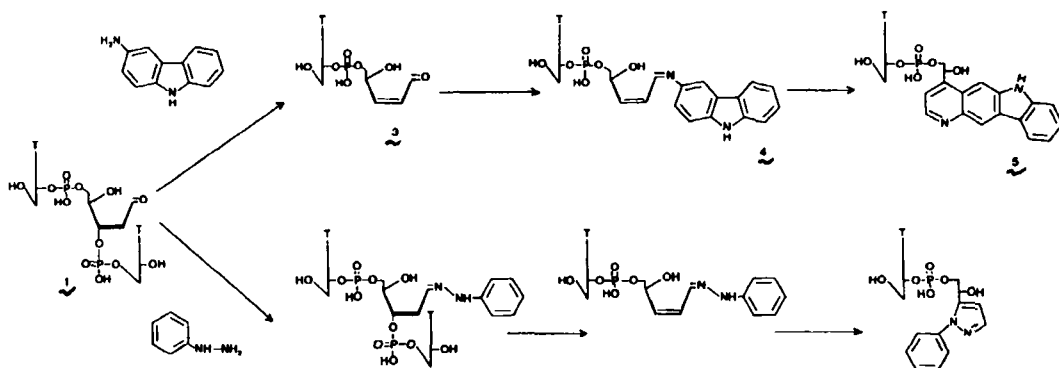


tion and cleaved the purine glycosidic bond gave the desired apurinic model 1. Direct attempts to purify 1 were unsuccessful due to degradation.

Treatment of the crude compound with methoxyamine² gave a stable adduct 2 which was then easily purified by preparative HPLC. Upon treat-

ment of the methyloxime derivative 2 with acetaldehyde in acidic medium, the pure AP site 1 was obtained.

Analysis of the reaction between the model 1 and 3-aminocarbazole revealed a two step reaction : (1) formation of an α,β -unsaturated aldehyde 3 resulting from β -elimination of 5'-phosphate thymidine and characterized by its UV spectrum (maximum 222 nm); (2) subsequent formation of an α,β -unsaturated Schiff base 4. This second intermediate appears to incorporate aminocarbazole moiety on the basis of the UV absorption at 305 and 366 nm. Attempts to isolate 4 failed since it undergoes facile cyclisation to the (6H) pyrido [3,2-b] carbazole derivative 5 characterized with (FAB) mass spectrometry and high resolution $^1\text{H-NMR}$ spectroscopy.



These results contrast with those found in case of phenylhydrazine where β -elimination occurred after phenylhydrazone formation. In this case intermediates were characterized by their UV spectra based on the literature.¹

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