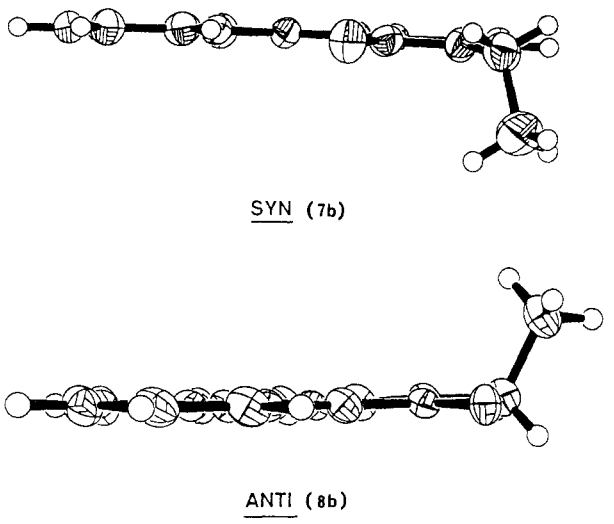

Figure 1. "End on" view of **7b** and **8b** (ORTEP plots) determined by X-ray analysis.

sp^3 center in the direction of a carbamate/imidazolide or amide/imidazolide intermediate, rotation about the original C4–C4a bond, and reclosure at the less hindered imidazolide nitrogen, N5, with formal loss of CH_3O^- or NH_3. The pyrimidinone ring opening and reclosure, which find some analogy in certain bicyclic[10,11] and tricyclic[12] systems, can be exploited as a reliable synthetic route to heretofore unavailable anti-disubstituted tetracyclic isomers based on a central 1,3,4,6-tetraazapentalene unit. Conditions were also found for the *O*-deprotection of **7a**, which preserved the syn ring system. Treatment of **7a** with 0.2 M *tert*-butylamine in methanol at −10 to −5 °C for 3 h yielded **7c** (79%), which retained the low-field signal (δ 9.13) of the 10-H in the vicinity of the carbonyl oxygen in the bay region. Deprotection conditions can thus be adjusted to produce either syn or anti isomers.

Finally, since structure **6c** represents an extended 1,N^6-ethenoadenosine system, the corresponding fluorescent 5′-di- and -triphosphates may be interesting candidates, like ϵADP and ϵATP,[13] for the examination of coenzyme–enzyme interactions.[14]

Acknowledgment. The work was supported by research grant CHE 84-16336 from the National Science Foundation. This paper is dedicated to Professor Michinori Ōki, University of Tokyo, now at Okayama University of Science, Japan, on the occasion of his 60th birthday.

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Received December 30, 1988

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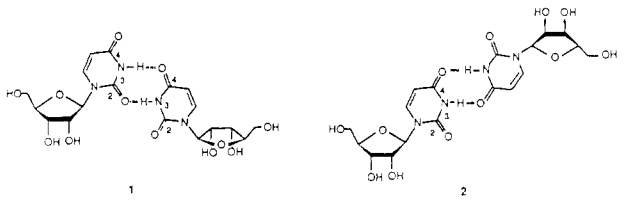
Syn to Anti Rearrangement of Dipyrimidinone-Substituted 1,3,4,6-Tetraazapentalenes. A Covalently Linked Cross Section Representative of Base Pairing in a Double-Helical Polynucleotide Having Parallel Strands

Summary: The syn to anti conversion of dipyrimidinone-substituted 1,3,4,6-tetraazapentalenes with base provides a covalently linked cross section that is a model for base pairing in a double-helical polynucleotide having parallel strands.

Sir: Until now, there has not been available a well-defined cross section that fixes a double-helical RNA in a reversed mode, that is, with parallel rather than antiparallel strands. Asymmetrical hydrogen bonding between two uridine moieties (1), involving N^3–H···O^4 and O^2···H–N^3 bonding, has been observed in crystalline UpA by X-ray analysis.[1] A "short base pair" between uridine and cytidine, involving O^4···H–N^4, and N^3–H···N^3 bonding, remains hypothetical, but a covalently linked pyrimidine–pyrimidine model of this has been synthesized,[2] thus providing a dimensionally equivalent analogue of a "pinched-in" RNA cross section. Among the possible hydrogen-bonding patterns between two uridine moieties that have been considered,[3] symmetrical bonding involving O^4···H–N^3 and N^3–H···O^4 (2) base pairing would lead to a polynucleotide double helix with parallel strands.



1 2

The syn to anti rearrangement of disubstituted 1,3,4,6-tetraazapentalenes described in the preceding paper[4] has made it possible for us to synthesize a covalently linked cross section with molecular architecture similar to **2**. First, a simplified version was constructed. The heating of 1-ethylcytosine (**3**)[5] (0.50 g, 3.6 mmol) and chloroketene diethyl acetal (**4**) (0.27 g, 1.8 mmol) in anhydrous DMF–benzene (2 mL each) at 90 °C for 24 h,[6] followed by solvent removal under vacuum, radial chromatography on silica gel,[7] and recrystallization from ethanol, yielded compound **5** (0.107 g, 20%), mp 240 °C R_f 0.27 (10% MeOH–$CHCl_3$).

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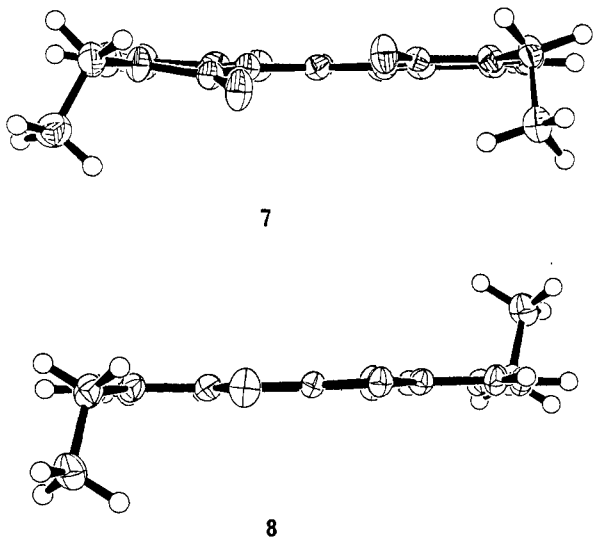
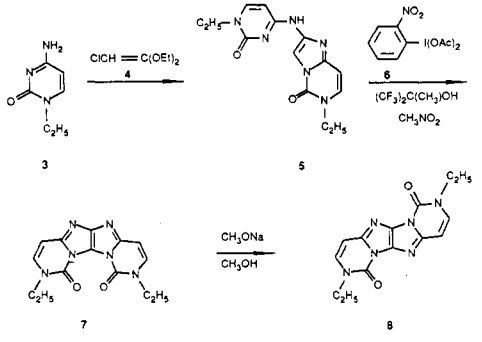
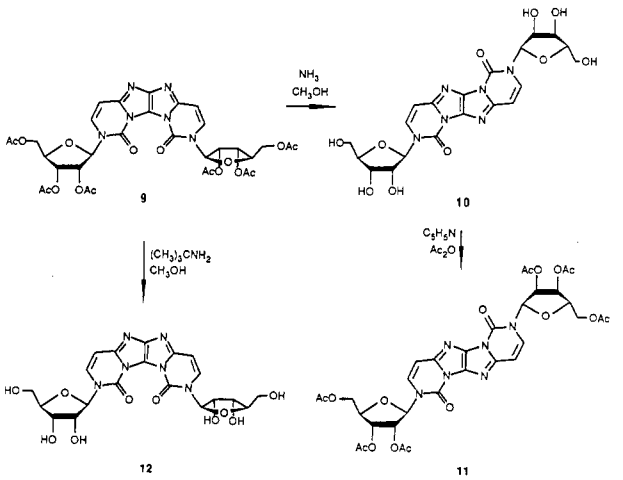


Figure 1. "End on" view of **7** and **8** (ORTEP plots) determined by X-ray analysis.

The structure was confirmed by ^{1}H NMR, low-resolution FABMS, and microanalysis. Oxidative cyclization of this intermediate was achieved with 2-nitro(diacetoxyiodo)-benzene (**6**)[2,8] in $(CF_3)_2C(CH_3)OH/CH_3NO_2$ to give compound **7**, which was purified by flash chromatography on silica gel, elution with 3–5% MeOH–$CHCl_3$, followed by recrystallization from methanol: yield, 54%; mp 281–282 °C; FABMS m/z 299 $(M + 1)^+$; R_f 0.47 (10% MeOH–$CHCl_3$). The structure of compound **7** was confirmed by ^{1}H NMR spectroscopy, which indicated symmetry in the molecule, by elemental analysis, and finally by X-ray crystallography.[9] A syn to anti rearrangement was effected with 0.4 M $NaOCH_3$ in methanol to give the isomeric $C_{14}H_{14}N_6O_2$ product **8**: yield, 74%; mp >300 °C; FABMS m/z 299 $(M + 1)^+$; R_f 0.60. The proton NMR spectra of **7** and **8** were similar, but the UV absorption spectra differed. In methanol, the longest UV absorption maximum for the syn isomer (**7**) was at 351 nm whereas that for the anti isomer (**8**) was at 362 nm and more intense. Final confirmation of the structure of the anti compound was obtained by X-ray analysis.[9] The most interesting structural features are shown in the "end on" views of **7** and **8** (Figure 1): for **7**, the out-of-plane avoidance of the carbonyl oxygens, the warped ring structure, and the occurrence of the ethyl groups on the same side of the molecule in the crystal; for **8**, the essentially planar ring structure, with the ethyl groups on opposite sides of the tetracyclic ring plane.



When compound **9**,[2] which was synthesized by the same route as **7**, starting with 2′,3′,5′-tri-*O*-acetylcytidine, was treated under more vigorous conditions than the previously described deblocking procedure,[2,10] namely, methanolic ammonia at 30 °C for 24 h, a single deprotected product, $C_{20}H_{22}N_8O_{10}$, mp 242–243 °C, was obtained in 90% yield. Its structure was established as anti (**10**) by reacetylation almost quantitatively with Ac_2O/pyridine at room temperature during 12 h to give the fully acetylated derivative, mp 192–193 °C. This could be safely assigned the related structure **11**, since the low- and high-resolution FAB mass spectra and the ^{1}H NMR spectrum together determined the composition, and the R_f was different (0.70) from the R_f for **9** (0.53) while the longest wavelength UV absorption maximum in methanol was 362 nm versus 351 for **9**. Compound **9** was successfully deacetylated with complete retention of the syn geometry by the use of 0.2 M *tert*-butylamine in methanol at −5 to −10 °C for 2 h (74% yield). It is best to use relative R_f's and UV maxima to differentiate between **9** and **11** and between **8** and **12** since the ^{1}H NMR spectra of the related pairs are strikingly similar.



With the versatile methodology described in this paper, it is possible to obtain pure syn and anti isomers, like **12** and **10**. The latter corresponds to a covalently linked cross section representative of base pairing in a double-helical polynucleotide with parallel strands. Its geometry and fluorescence properties make it an attractive unit for possible intercalation and polynucleotide sequence incorporation.

Acknowledgment. This work was supported by research grant CHE 84-16336 from the National Science Foundation. This paper is dedicated to Professor Michinori Ōki, University of Tokyo, now at Okayama University of Science, Japan, on the occasion of his 60th birthday.

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(9) The X-ray data were obtained by Dr. Scott R. Wilson. Complete single crystal X-ray data of **7** and **8** will be provided in a full paper.
(10) In ref 2, even under the very mild conditions used to deprotect the hexaacetyl derivative, i.e., methanolic ammonia at 0 °C for 3 h, some contamination of the intended syn product with the anti isomer occurred.