Scheme I

$$\underset{1}{RCHO} + \underset{2}{BrCH_2X} + \underset{3}{(PhO)_3P} \xrightarrow[\text{THF–CH}_3\text{CN, room temperature}]{n\text{-Bu}_3\text{As (cat.), K}_2\text{CO}_3\text{(s)}} \underset{4}{RCH{=}CHX} + (PhO)_3PO$$

a, X = CO_2CH_3; b, X = C(O)Ph.

Table I. Reaction of Various Aldehydes with Methyl Bromoacetate (2a) and with ω-Bromoacetophenone (2b)

entry	1, R =	2	reactn time, h	isoltd yield, %	$E:Z^b$
1	p-ClC_6H_4	*a*	18	87	98:2
2	C_6H_5	*a*	30	86	99:1
3	o-ClC_6H_4	*a*	12	81	98:2
4	p-tolyl	*a*	24	80	98:2
5	n-C_5H_{11}	*a*	31	64	100
6	2-furyl	*a*	16	80	99:1
7	2-thiophenyl	*a*	17	75	97:3
8	2-pyridyl	*a*	17	68	99:1
9	PhCH=CH	*a*	18	61	E,E > 97
10	p-ClC_6H_4	*b*	24	75	>98
11	2-furyl	*b*	18	86	>98
12	n-C_4H_9	*b*	12	80	>98

[a] All the products were characterized by ^{1}H NMR. [b] The ratio of $E:Z$ isomer was determined by capillary GC.

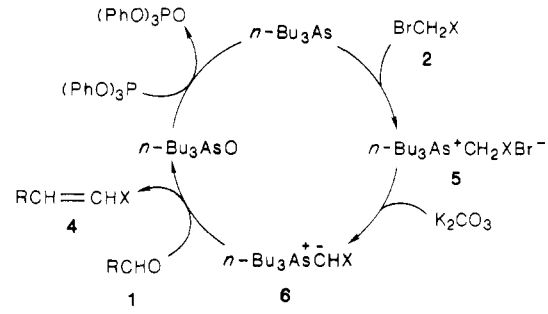
catalytic process has ever appeared in the literature. Herein we report the first example in this respect as summarized in Scheme I and Table I. A mixture of aldehyde (1 mmol), potassium carbonate (1.2 mmol), methyl bromoacetate (1.2 mmol), 0.5 mL of THF, 4 mL of acetonitrile, tributylarsine (0.2 mmol), and triphenyl phosphite (1.2 mmol) were stirred in a reaction tube under nitrogen at room temperature. After the reaction was completed (monitored by TLC), ethyl acetate was added. The resulting mixture was passed through a short column of silica gel to remove the inorganic salt. The desired product was obtained by flash chromatography.

The reaction path is proposed as shown in Scheme II.

Reaction of tri-n-butylarsine with bromo compound **2** forms arsonium salt **5**, which, in the presence of potassium carbonate, generates **6** in situ. Ylide **6** reacts with the aldehyde rapidly to afford the desired olefin **4**, and the tri-n-butylarsine is regenerated by reduction of tri-n-butylarsine oxide with triphenyl phosphite.

(16) Care should be taken for handling tri-n-butylarsine and the experiment should be carried out in an efficient hood.

Scheme II



The simplicity of our procedure, the mildness of the reaction conditions, the good yields, the high stereoselectivity, and especially the use of a catalytic amount of tri-n-butylarsine, demonstrates our method to be practical for the synthesis of α,β-unsaturated esters and ketones. Thus, our method provides the first example of a catalytic Wittig-type reaction. The extension of our method to the application of other elementoorganic compounds of nontransition elements in organic synthesis is being actively pursued.

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Registry No. **1** (R = p-ClC_6H_4), 104-88-1; **1** (R = C_6H_5), 100-52-7; **1** (R = o-ClC_6H_4), 89-98-5; **1** (R = tolyl), 104-87-0; **1** (R = C_5H_{11}), 66-25-1; **1** (R = 2-furyl), 98-01-1; **1** (R = 2-thiophenyl), 98-03-3; **1** (R = 2-pyridyl), 1121-60-4; **1** (R = PhCH=CH), 104-55-2; **1** (R = C_4H_9), 110-62-3; **2a**, 96-32-2; **2b**, 70-11-1; **3**, 101-02-0; (*E*)-**4** (R = p-ClC_6H_4, X = CO_2CH_3), 20754-21-6; (*E*)-**4** (R = C_6H_5, X = CO_2CH_3), 1754-62-7; (*E*)-**4** (R = o-ClC_6H_4, X = CO_2CH_3), 98288-14-3; (*E*)-**4** (R = tolyl, X = CO_2CH_3), 20754-20-5; (*E*)-**4** (R = C_5H_{11}, X = CO_2CH_3), 7367-81-9; (*E*)-**4** (R = 2-furyl, X = CO_2CH_3), 58293-85-9; (*E*)-**4** (R = 2-thiophenyl, X = CO_2CH_3), 119680-91-0; (*E*)-**4** (R = 2-pyridyl, X = CO_2CH_3), 81124-45-0; (*E*)-**4** (R = PhCH = CH, X = CO_2CH_3), 24196-39-2; (*E*)-**4** (R = p-ClC_6H_4, X = C(O)Ph), 22252-16-0; (*E*)-**4** (R = furyl, X = C(O)Ph), 39511-12-1; (*E*)-**4** (R = C_4H_9, X = C(O)Ph), 64235-53-6; Bu_3A_5, 5852-58-4.

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Pyrimidinone Ring Opening and Reclosure on a 1,3,4,6-Tetraazapentalene System: Syn to Anti Isomerization

Summary: Under nucleophilic attack, pyrimidinone ring opening and reclosure on syn-disubstituted 1,3,4,6-tetraazapentalenes effects syn to anti isomerization of the ring systems.

Sir: The discovery of an oxidative cyclization route to *syn*-dipyrido-substituted 1,3,4,6-tetraazapentalenes (e.g., **1**)[1,2] has led to the synthesis of covalently linked DNA/RNA cross sections representative of purine–pyrimidine, purine–purine, and pyrimidine–pyrimidine duplexes.[3,4] The synthetic methodology has now been applied to hybrid examples that are monopyrido-substituted 1,3,4,6-tetraazapentalenes. Those that have additional *syn*-pyrimidinone substitution are susceptible to pyrimidinone ring opening and reclosure on the 1,3,4,6-tetraazapentalene system, which results in overall syn to anti isomerization. While the rearrangement and isomerization are of intrinsic

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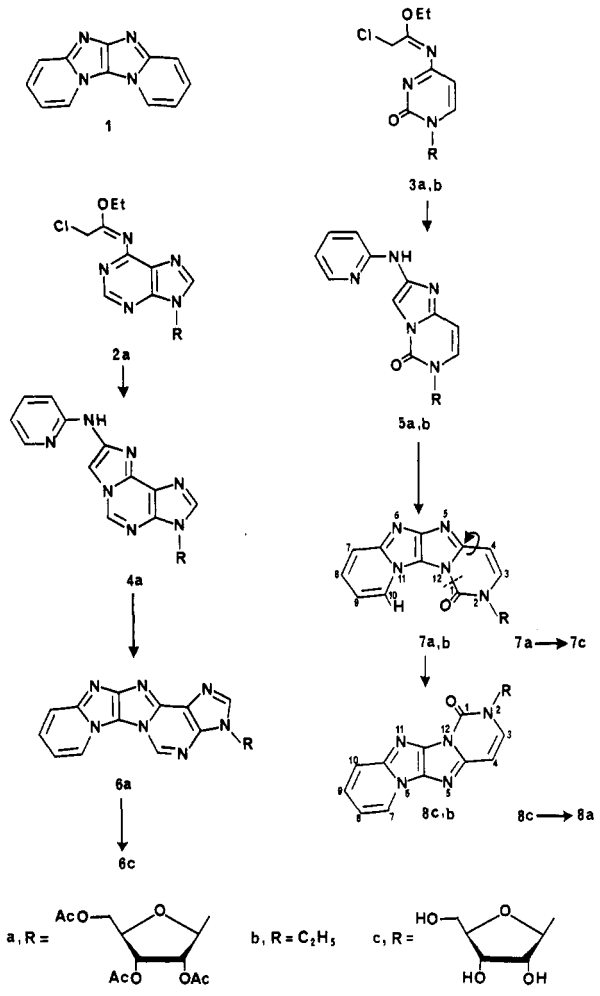
Scheme I



interest, they also provide a unique and at the same time effective synthetic route to anti-disubstituted 1,3,4,6-tetraazapentalenes.

The synthesis of the desired pentacyclic and tetracyclic tetraazapentalenes is outlined in Scheme I for the purine and pyrimidine series. N^6-(1-Ethoxy-2-chloroethylidene)-2′,3′,5′-tri-*O*-acetyladenosine (**2a**)[3,5] and N^4-(1-ethoxy-2-chloroethylidene)-2′,3′,5′-tri-*O*-acetylcytidine (**3a**)[4,5] were heated separately with 2-aminopyridine to afford the intermediates **4a** (42%), mp 194 °C, and **5a** (21%), mp 166–167 °C, respectively. The structure of **4a** was indicated by low- and high-resolution FAB mass spectrometric data and by the NMR chemical shift of the original 2-proton on the purine nucleus in **2a**, which moved to lower field[3,5] by 0.6 ppm on ring closure. The structure of **5a**, with the creation of the etheno bridge on the cytidine side rather than the pyridine side of the system, was indicated by the usual spectroscopic criteria and by the marked downfield shift (0.93 ppm) of the original 5-H of the cytidine moiety, upfield shift (0.15 ppm) of the original 6-H, and corresponding net decrease in chemical shift difference between the pyrimidine ring protons.[4,5]

Oxidative cyclization of **4a** with (diacetoxyiodo)benzene in trifluoroethanol[1-4] yielded (55%) the pentacyclic N-heteroaromatic ring structure **6a**, mp 227–228 °C. Similar treatment of **5a** yielded (50%) the tetracyclic N-heteroaromatic ring structure **7a**, mp 140–143 °C. The structures were confirmed by microanalytical, low- and high-resolution FAB mass spectral, and ^{1}H NMR spectral data.

(5) Leonard, N. J.; Cruickshank, K. A. *J. Org. Chem.* **1985**, *50*, 2480.

O-Deprotection of **6a** under the usual conditions, i.e., methanolic ammonia at 30 °C, yielded (75%) 3-(β-D-ribofuranosyl)-3*H*-pyrido[1″,2″:1′,2′]imidazo[4′,5′:4,5]-imidazo[2,1-*i*]purine (**6c**), mp 270–271 °C. The composition of **6c** was confirmed by low- and high-resolution FAB mass spectra. The ring structure remained the same as in **6a** as shown by the nearly identical chemical shifts for the aromatic protons in the ^{1}H NMR and by the matching UV spectra in the region 238–350 nm for **6a** and **6c**.

When compound **7a** was treated with methanolic ammonia under the same conditions, a colorless solid resulted that exhibited a molecular ion at m/z 358 (MH^+) in the FABMS, satisfactory for the *O*-deprotected compound. However, the ^{1}H NMR spectrum was indicative of the presence of two ribonucleosides of very similar structure. Reacetylation of this product with Ac_2O/pyridine gave a mixture of two compounds that could be more readily separated by thin-layer silica gel chromatography (10% MeOH/$CHCl_3$). The compound with the lower R_f value (0.52) corresponded to **7a** while that with the higher R_f (0.67) showed the same molecular ion, m/z 484 (MH^+), in the FABMS and one marked difference among the ^{1}H NMR signals. The resonance at δ 9.09 for **7a**, which corresponded to the proton at C-10, deshielded by the paramagnetic anisotropy[6] of the proximal carbonyl group in the bay region, was shifted upfield by 0.35 ppm to 8.74 in the second compound.

The behavior of a simplified version (**7b**) of **7a** was examined to exclude possible complications of separation and characterization resulting from the presence of the ribofuranosyl moiety. Compound **7b**, mp 261–262 °C, FTIR 1680.2 cm^{-1}, was made by oxidative cyclization (50% yield) of **5b** with (diacetoxyiodo)benzene in trifluoroethanol. The precursor **5b** was prepared (30% yield) by the condensation of N^4-(1-ethoxy-2-chloroethylidene)-1-ethylcytosine (**3b**) with 2-aminopyridine. Compound **3b** had resulted from an initial reaction of 1-ethylcytosine[7] with chloroketene diethyl acetal (80% yield) in acetonitrile at 30 °C during 20 h. Treatment of **7b** with ammonia in methanol at room temperature for 24 h gave a product with a higher R_f value (0.62) than the original (0.55) in TLC on silica gel, 10% MeOH/$CHCl_3$ as solvent. Recrystallized from methanol, the new product, $C_{13}H_{11}N_5O$, mp 279–280 °C, FTIR 1686.0 cm^{-1}, was isomeric with **7b** and differed spectroscopically (e.g., longest UV λ_{max} 374 vs 364 nm (CH_3OH) for **7b**). The major difference was the upfield shift, by 0.39 ppm, of the proton magnetic resonance from δ 9.12 in **7b** to 8.73 ppm in the new compound, similar to the change in the ribosyl case. A more rapid conversion was realized when ammonia in methanol was replaced by 0.4 M $NaOCH_3$ in methanol.

The products of treatment of **7a** and **7b** under the basic conditions described thus have the anti[8] structures **8c,b** based upon the major significant changes in ^{1}H NMR spectra in the course of the rearrangement, along with additional analytical and spectroscopic data, including X-ray analysis of **7b** and **8b**.[9] The syn isomer has a slightly warped ring structure while the anti isomer has an essentially planar ring structure (Figure 1). The plausible reaction pathway involves nucleophilic attack at the carbonyl by CH_3O^- or NH_3, fragmentation at the new

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(9) The X-ray data were obtained by Dr. Scott R. Wilson. Complete single crystal X-ray data of **7b** and **8b** will be provided in a full paper.

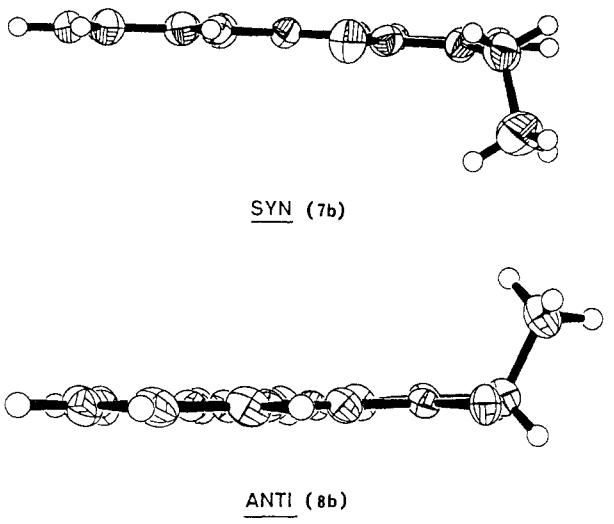

Figure 1. "End on" view of **7b** and **8b** (ORTEP plots) determined by X-ray analysis.

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]

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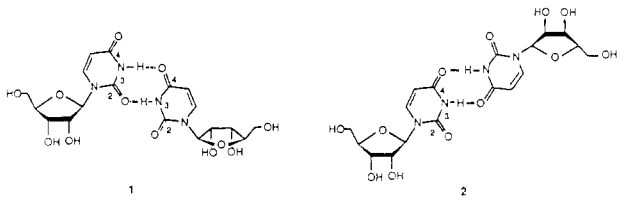
Syn to Anti Rearrangement of Dipyrimidinone-Substituted 1,3,4,6-Tetraazapentalenes. A Covalently Linked Cross Section Representative of Base Pairing in a Double-Helical Polynucleotide Having Parallel Strands

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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