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Poly(U)-Directed Transamidation between Adenosine 5′-Phosphorimidazolide and 5′-Phosphoadenosine 2′(3′)-Glycine Ester

Sir:

Many derivatives of adenosine form organized triple-helical structures with polyuridylic acid (poly(U)) in which one column of molecules of the adenosine derivative is held in position by two chains of poly(U).[1] We have shown that adenosine 5′-phosphorimidazolide (ImpA) forms such a structure at 0°, and then undergoes template-directed polymerization to form short 2′–5′-linked oligoadenylic acids.[2] More recently we have confirmed that the 2′(3′)-glycyl ester of adenosine 5′-phosphate (pA-Gly) forms a similar helix melting at 17.5°[3] and have discovered a novel template-directed reaction between ImpA and pA-Gly.

We prepared two mixtures (pH 7.0), each containing 0.0125 *M* ImpA-**8**-^{14}C (specific activity 0.8 mCi/mmol), 0.0125 *M* pA-Gly, 0.075 *M* $MgCl_2$, and 0.20 *M* NaCl. Mixture 1 contained in addition 0.05 *M* poly(U), while mixture 2 served as a template-free control. The mixtures were held at 0° and their pH's maintained at 7.0 by titration with NaOH. Aliquots were withdrawn at various times for analysis. Each aliquot was subjected to electrophoresis in a 0.03 *M* potassium phosphate buffer (pH 7.1) and to chromatography in system I, 1-propanol–concentrated ammonia–water (55:10:35, v/v), and system II, 95% ethanol–1 *M* ammonium acetate (pH 7.5) (7:3, v/v).

In reaction 2 we observed a slow disappearance of ImpA, and the appearance of two new radioactive compounds which we readily identified as adenylic acid (pA) and P_1P_2-diadenosine 5′-pyrophosphate (AppA).[4] In reaction 1 we noted a much more rapid disappearance of ImpA and the appearance of a major new radioactive product (compound I) which failed to move from the origin on chromatography in system II, and had an electrophoretic mobility of 0.85 on electrophoresis at pH 7.1 (adenosine, 0.0; pA, 1.0). In the ammonia-containing system I, a mixture of radioactive adenylyl-(5′ → *N*)-glycine (Gly-N-pA) and adenylyl-(5′ → αN)-glycinamide ($NH_2C(=O)CH_2NHpA$) was formed in a total amount that roughly corresponded to the yield of compound I determined in the other systems.

These observations clearly point to the structure pA-2′(3′)-Gly-N-pA for compound I. This was confirmed by showing that it yielded equimolar amounts of pA and Gly-N-pA when treated with aqueous alkali (pH 12, 20°, 4.5 hr). The hydrolysis products pA and Gly-N-pA were identified by paper chromatography in system II and in a mixture of isopropyl alcohol–concentrated NH_4OH–H_2O (7:1:2), as well as by electrophoresis at pH 7.1. Furthermore, compound I could be prepared by the action of a water-soluble carbodiimide (1-ethyl-3-dimethylaminopropylcarbodiimide hydrochloride) on an aqueous solution containing equimolar quantities of pA and Gly-N-pA, with or without poly(U), but preferably in the presence of imidazole buffer (see below).

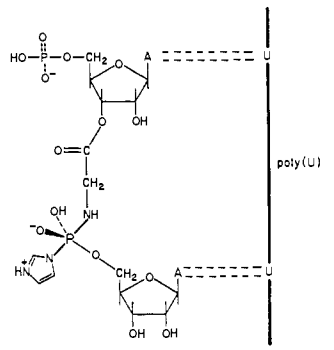
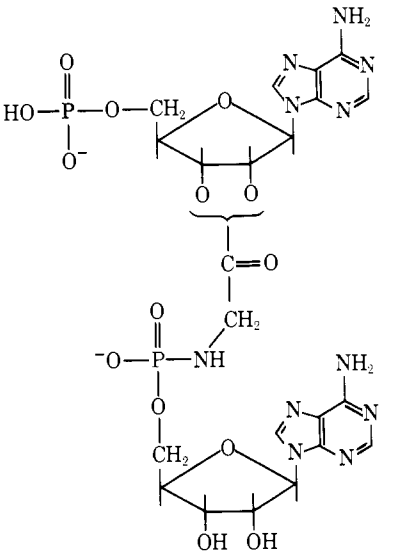


Figure 1. Proposed transition state for the template-directed transamidation reaction. The broken lines joining A and U represent Watson–Crick hydrogen bonds. A second poly(U) chain has been omitted in order to simplify the diagram.



Our quantitative studies showed that after 2 hr at 0° the yield of compound I was 55.8% in reaction 1 and 1.5% in reaction 2. After 24 hr the yields were 79.1 and 5.2%, respectively. These results demonstrate that the incorporation of pA-Gly and ImpA in an organized helix with poly(U) brings the NH_2 group of glycine sufficiently close to the phosphate residue of ImpA to permit a relatively rapid transamidation reaction at 0° (Figure 1). In our experiments the template increased the rate of reaction by a factor of at least 35. This ratio has no particular significance—it would be larger in more dilute solutions and smaller in more concentrated solutions.

The carbodiimide-induced condensation of Gly-N-

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pA with pA was facilitated slightly by the presence of poly(U) but much less than the transamidation reaction. Poly(U) did, however, stabilize compound I against hydrolysis, presumably through the formation of a triple helix. We used a solution containing 0.0125 *M* [8-^{14}C]-pA (specific activity 0.32 mCi/mmol), 0.0125 *M* Gly-N-pA, 0.075 *M* $MgCl_2$, 0.2 *M* NaCl, and 0.125 *M* carbodiimide. After 3 days at 0° and at pH 7.0, we obtained a 5.5% yield of compound I in the absence of imidazole or poly(U), a 9.5% yield in the presence of 0.05 *M* poly(U), a 23.5% yield in the presence of 0.125 *M* imidazole buffer, and a 43.5% yield in the presence of both poly(U) and imidazole. We believe that the carbodiimide activates the carboxyl group of Gly-N-pA and that the activated carboxyl derivative is rapidly converted to an imidazolide. The imidazolide then reacts selectively with the OH groups of pA.[5]

It is not clear whether the template-directed transamidation reaction has any prebiotic significance. We anticipate that compounds of the type ImpA-2′(3′)-Gly will undergo template-induced polymerizations to give oligomers that could be interesting in this context.

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(5) R. Saffhill and C. K. Biebricher, unpublished results.

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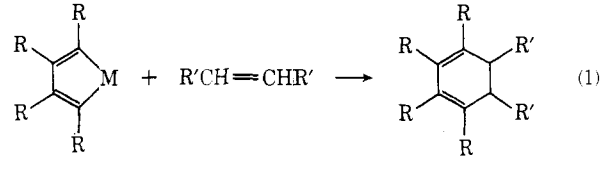
Cobaltacyclopentene Complex as an Intermediate in Cobalt-Catalyzed Cooligomerization of Diphenylacetylene with Cyano Olefins

Sir:

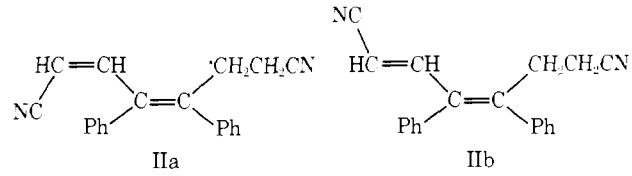
The catalysis of the oligomerization of acetylenes, especially cyclotrimerization, by transition metal complexes has been extensively studied, but only a few examples of the cooligomerization of acetylenes with olefins have been noted.[1] The linear and cyclo trimerization of two molecules of acetylene with one molecule of olefin have been catalyzed by $NiBr_2(PPh_3)_2$, $Ni(CO)_2(PPh_3)_2$, and other nickel catalysts.[2] Although the reaction mechanism is not clear in these systems, some suggest one which involves metallo cyclopentadiene intermediacy, as in eq 1.[2a-e]



(1)

In the course of our studies on the cobalt-catalyzed synthesis of pyridines from acetylenes and nitriles,[3] we have found that diphenylacetylene cooligomerizes with some cyano olefins. In the present communication, we report this new type of cooligomerization and propose a mechanism involving a novel intermediate.

The reaction of diphenylacetylene with acrylonitrile in benzene at 70° in the presence of π-$C_5H_5Co(PPh_3)(PhC{\equiv}CPh)$ (I) gives colorless crystals with the composition $(PhC_2Ph)(CH_2CHCN)_2$ (II) in 560% yield based on I. This compound is a 1:1 mixture of two isomers which were separated by chromatography on alumina: IIa, mp 126–128°; IIb, mp 101.5–102°. On the basis



of pmr spectra, the structures illustrated were assigned to these compounds.

When π-$C_5H_5Co(PPh_3)(PhC{\equiv}CCO_2Me)$ (III) is used instead of I, the catalytic reaction does not proceed, probably owing to the formation of stable intermediates; indeed the reaction of III with acrylonitrile at room temperature affords stable diene complex IV, 155–157° dec, in 16% yield.

The reaction of III with dimethyl maleate in benzene at room temperature gives a 30% yield of red crystalline complex V, 177–178° dec, isolated by chromatography and purified by crystallization from dichloromethane–hexane. The structure of this compound has been established by a single-crystal X-ray analysis. Crystal data are: $a = 12.330$, $b = 17.834$, $c = 8.955$ Å; $\alpha = 98.12$, $\beta = 116.13$, $\gamma = 81.13°$; $V = 1741$ Å^3; $d_{measd} = 1.36$, $d_{calcd} = 1.359$ g/cm^3 (assuming 0.25 mol of CH_2Cl_2 per mole of complex) for $Z = 2$; space group $P\bar{1}$. The structure determination was based on 4673 independent reflections, collected on a Rigaku four-circle automatic diffractometer using Cu Kα radiation monochromated from graphite. The block diagonal least-squares refinement converged to a conventional *R* value of 10.6%. The molecule consists of a cyclopentadienyl group, triphenylphosphine, and cobaltacyclopentene ring (Figure 1). The cobalt atom and C(1), C(2), and C(3) are in a same plane with C(4) bent from this plane by 34.2°.

The formation of metallocycles is an important feature of this type of acetylene complex; the reactions of I with acetylenes,[4] carbon disulfide, and carbonyl sulfide[5] have been known to yield respective five-membered metallocyclic complexes. Complex V cannot be obtained by the reaction of π-$C_5H_5Co(PPh_3)(MeO_2CCH{=}CHCO_2Me)$ with $PhC{\equiv}CCO_2Me$.

The treatment of complex V with acrylonitrile (70°) or diphenylacetylene (room temperature) in benzene affords red crystalline diene complexes VI and VII (Scheme I) in 17 and 46% yield, respectively.

These model reactions imply the mechanism shown in Scheme II for the catalytic cooligomerization reaction. The primary step of the proposed mechanism is the formation of the cobaltacyclopentene complex analogous to V. The second step is the displacement of triphenylphosphine by acrylonitrile followed by the transfer

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