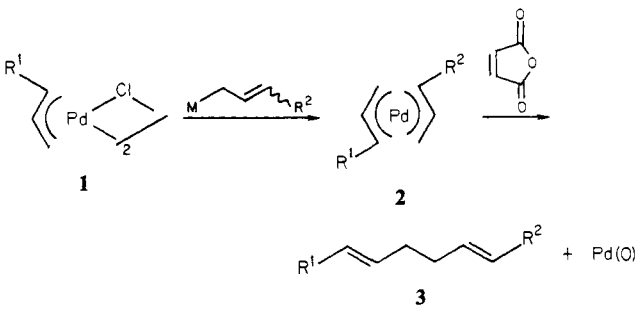
Scheme I



temperature. The reaction mixture was filtered, and products were isolated in a combined yield of 92%. No coupled product was obtained in the absence of maleic anhydride in which case all of **1c** was converted to diene and olefins. Without dioxane, only 2% of cross-coupled material was obtained; the predominant products of coupling were derived from crotyl groups exclusively (Table I).

The stereochemistry of coupling was established by examination of products **3f-1** and **3f-2** prepared from (η^3-allyl)palladium complex **1f** in which the palladium moiety is trans to the methoxy substituent.[8] Compound **3f-1** was assigned a trans stereochemistry by ^{1}H NMR[8,9] as was **3f-2**. That carbon–carbon bond formation occurs on the same face of the η^3-allylic unit as that one to which the palladium was attached substantiates the notion that carbon–carbon bond formation occurs via a sequence of transmetalation and reductive elimination.[10,12]

Methods other than π-acidic ligand coordination could induce reductive elimination from **2**, and a series of oxidative procedures were therefore examined. Cyclic voltammetric analysis of bis(allyl)palladium(II) and bis(crotyl)palladium(II) showed an irreversible oxidation at −0.85 and −1.25 V (vs. SCE), respectively. Preparative electrochemical techniques or 1e$^-$ oxidants were utilized to induce elimination from bis(allylic)palladium(II) species;[13] however, low yields and selectivities of products resulted (see Table II). Significant amounts of byproduct allylic chloride and allylpalladium chloride were obtained when Na_2IrCl_6 was used as the oxidant suggesting a radical decomposition or a competition between bona fide reductive elimination and radical decomposition (the existence of radical decomposition pathways has been noted in oxidation of diorganoiron,[14] -nickel,[15] and -platinum species[16]).[17]

That complementary regiochemistries for carbon–carbon bond formation can occur for reactions between (allyl)palladium halides and other allylic metallic species, depending on the choice of a direct attack[2i,j] or a transmetalation sequence, gives the synthetic chemist a satisfactory degree of control in allylic–allylic cross-coupling sequences in which "head" and "tail" of the allylic units are sterically clearly different.

Acknowledgment. We acknowledge support for this work given by the National Institutes of Health and the National Science Foundation.

(8) Bäckvall, J.; Nordberg, R. E.; Zetterberg, K.; Åkermark, B. *Organometallics* **1983**, *2*, 1625.

(9) Stereochemical assignments were made by a series of decoupling and NOE experiments; for the protons on methoxy-substituted carbon and on the adjacent methylene carbon, for **3f-1** J = 8.4 Hz and for **3f-2** J = 8.9 Hz.

(10) Selective attachment at C(20) occurs in maleic anhydride induced coupling between a steroid-derived (η^3-allylic)palladium complex and an *alkenyl*zirconium reagent.[1a] An analogous procedure using an *allylic* Grignard gave coupling almost exclusively at C(16) with side-chain attachment determined to be α by ^{13}C and ^{1}H NMR comparison with authentic material; for the C(20) coupled product, the *R* configuration was obtained. Thus, in both cases, product is formed by transmetalation–reductive elimination. This change in coupling selectivity may be due to a fixed (η^3-allylic)palladium-(η^1-alkenyl) configuration in the first case,[1a] a geometrically labile bis(allylic)palladium complex[11] in the latter, and the possible existence of competing direct and conjugate coupling mechanisms for bis(allylic)palladium species.

(11) A number of syn–anti isomers are possible. As well, for **2b**, ^{1}H NMR analysis suggests the presence of an (η^3-allyl)(η^1-allyl) isomer: at −60 °C δ (CD_2Cl_2) 4.75–5.20 (m, 2 H), 1.78 (br s, 3 H), 1.06 (d, d, 2 H).

(12) Other π-acidic ligands (e.g., fumaronitrile or benzoquinone) were also successfully employed.

(13) Both discrete **2** and $P(CH_3)_3$ adducts of **2** (to give an η^3, η^1, PMe_3 species) were utilized. Low-temperature NMR of the latter was identical with that reported: Wilke, G.; et al. *J. Organomet. Chem.* **1980**, *191*, 449.

(14) Kochi, J. K.; Lau, W.; Huffmann, J. C. *Organometallics* **1982**, *1*, 155.

(15) Almemark, M.; Åkermark, B. *J. Chem. Soc., Chem. Commun.* **1978**, 66.

(16) Chen, J. Y.; Kochi, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 1450.

(17) The presence of the free radicals was further substantiated by their being trapped by O_2.

Stereoselective Aminoacylation of Polyribonucleotides

Albert T. Profy and D. A. Usher*

Department of Chemistry, Cornell University
Ithaca, New York 14853

Received February 6, 1984

Contemporary proteins contain only L-amino acids, and nucleic acids contain only D nucleosides, but the pathway for the coevolution of the chirality of these molecules is unknown. With present-day aminoacyl-tRNA synthases the L-amino acid generally is linked to the 3′ end of the tRNA molecule more rapidly than the D isomer,[1] but simple *chemical* aminoacylation at the 3′-terminus of a dinucleoside monophosphate was found to be chirally nonselective.[2] Thus the observation of chiral selection in a nonenzymatic reaction that yields aminoacyl esters of RNA may be of potential importance for reconstructing the evolution of this chiral specificity.

We now report that the reaction of racemic [*N*-(3,5-dinitrobenzoyl)-DL-alanyl]imidazole with D-poly(adenylic acid) (poly(A)), poly(uridylic acid) (poly(U)), poly(cytidylic acid) (poly(C)), or poly(inosinic acid) (poly(I)) resulted in the preferential acylation of each polynucleotide by the L enantiomer of *N*-(3,5-dinitrobenzoyl)alanine. The stereoselective reaction appeared to take place on the "internal" 2′-hydroxyl groups, and the enantiomeric excess (ee) was usually 40–60%.

Polynucleotides were purchased from P-L Biochemicals and dialyzed for 2 days against 10 mM tris(hydroxymethyl)aminomethane buffer (pH 7.0) containing 1 mM ethylenediaminetetraacetic acid and then against 10 mM triethylammonium bicarbonate (pH 8.1). *N*-(3,5-Dinitrobenzoyl)-DL-alanine was prepared by the Schotten–Baumann procedure of Ronwin.[3] To form a 0.3 M solution of the imidazolide, this amino acid (10.3 mg, 36 μmol) was dissolved in 0.125 mL of dimethylformamide (DMF), 1,1′-carbonyldiimidazole (6.3 mg, 39 μmol) was added, and the solution was incubated for 30 min at room temperature.[4] A 0.6 M solution of the imidazolide in DMF was prepared similarly. The acylation of polynucleotides by both 5 and 10 equiv of imidazolide per nucleoside hydroxyl group was studied. The polymer (1.5 μmol in nucleoside units) in 75 μL of H_2O was treated with 25 μL of either the 0.3 or 0.6 M imidazolide solution. After a 1-h incubation at room temperature, the reaction mixture was applied to a 1.1 × 23.5 cm Bio-Gel P2 column (Bio-Rad Laboratories) and eluted with 0.1 M triethylammonium acetate (pH 6.4). The absorbance of the eluate was monitored at 248.5 nm, and the well-resolved fraction corresponding to the acylated polynucleotide was isolated and lyophilized. Each acylated polymer was treated with 0.1 N NaOH (1 h, room temperature), and the liberated *N*-(3,5-dinitrobenzoyl)-DL-alanine was purified by HPLC on an octadecylsilyl bonded-phase column using a 0.1 M ammonium acetate buffer (pH 4.7) and an acetonitrile gra-

(1) Calendar, R.; Berg, P. *J. Mol. Biol.* **1967**, *26*, 39–54. See also: Yamane, T.; Miller, D. L.; Hopfield, J. J. *Biochemistry* **1981**, *20*, 7059–7064. Tyrosyl-tRNA synthase appears to be a special case.

(2) Profy, A. T.; Usher, D. A. *J. Mol. Evol.* **1984**, *20*, 147–156. However, the equilibrium constant for the 2′ ⇌ 3′ aminoacyl migration reaction in inosinylylinosine does differ for D- and L-Boc-alanine.

(3) Ronwin, E. *J. Org. Chem.* **1957**, *22*, 1180–1182.

(4) Gottikh, B. P.; Krayevsky, A. A.; Tarussova, N. B.; Purygin, P. P.; Tsilevich, T. L. *Tetrahedron* **1970**, *26*, 4419–4433.

0002-7863/84/1506-5030$01.50/0

Table I

polymer	yield, %[a] 10:1[c]	yield, %[a] 5:1[c]	ee of L isomer, %[b] 10:1[c]	ee of L isomer, %[b] 5:1[c]
poly(A)	6	3	58	52
poly(I)	7	5	53	57
poly(U)	7	5	48	45
poly(C)	2	1	41	35

[a] Yields are reported as the percentage of mononucleotide units acylated by the imidazolide of *N*-(3,5-dinitrobenzoyl)-DL-alanine. [b] The enantiomeric excess (ee) of the polymer-bound *N*-(3,5-dinitrobenzoyl)alanine is defined as the % *L* isomer minus the % *D* isomer. Uncertainties are ±3%. [c] The ratio of reactants, (imidazolide):(nucleotide units).

dient.[5] The amino acid derivative was detected by its absorbance at 254 nm, and the acylation yield was determined from the chromatographic peak area using a molar absorptivity (254 nm) of 14.6×10^3 M^{-1} cm^{-1} (measured in 0.1 M NH_4OAc, pH 4.7, containing 20% acetonitrile). The enantiomers of the purified dinitrobenzoylalanine were separated by HPLC on a chiral stationary phase consisting of one enantiomer of 1-amino-1-(6,7-dimethylnaphth-1-yl)-2-methylpropane linked to a 5-μm silica matrix.[6] The derivatives were eluted with a mobile phase of 4:1 water/methanol containing 1 g/L $KHCO_3$ and 20 g/L K_2SO_4 and were detected by their absorbance at 254 nm. Relative amounts of the D and L enantiomers were determined from the chromatographic peak areas. Table I shows the percent of nucleoside hydroxyl groups that were acylated and the ee of the L isomer that was incorporated into each polymer. The reactant *N*-(3,5-dinitrobenzoyl)-DL-alanine was shown to be racemic (ee = 0 ± 3%) by HPLC on the chiral stationary phase.

Previously, polynucleotides have been acylated by the imidazolides of *N*-acetyl-L-amino acids and L-amino acid trifluoroacetates,[7-9] but in these experiments, no attempt was made to compare the behavior of D- and L-amino acid derivatives. We recently reported that aminoacylation of the "internal" 2'-hydroxyl group of a dinucleoside monophosphate (D-inosinylyl-D-inosine) by the imidazolide of racemic *N*-(*tert*-butoxycarbonyl)alanine resulted in the formation of excess L ester.[2] Since aminoacyl imidazoles are believed to acylate polyribonucleotides principally at the 2'-hydroxyl groups along the ribose backbone,[8,9] the preferential incorporation of (dinitrobenzoyl)-L-alanine into the polymers is consistent with the earlier work. The stereoselectivity appears to be somewhat lower for the pyrimidine polymers than for the purine polymers, possibly reflecting the smaller amount of secondary structure in the former. The overall yields of esters (Table I) were consistent with the reported relative rates of polymer acylation by *N*-acetylamino acid imidazolides, which decreased in the order poly(U) > poly(A) > poly(C).[7-9] Stereoselective diastereomer formation by amino acids has been reported previously,[10-14] but there appears to be no prior case involving the aminoacylation of a nucleic acid.

Derivatives of amino acids have been shown to interact stereoselectively with polynucleotides. Gabbay et al.[15] found that *N*-(L-aminoacyl)diaminoethanes stabilized RNA double helices to a greater extent than did the D-amino acid derivatives, while the D isomers afforded single-stranded polymers greater protection against hydrolysis by ribonucleases.[16] Similarly, L-lysyl-L-amino acid dipeptides stabilized double-helical complexes more than did the corresponding L-lysyl-D-amino acid diastereomers.[15] These noncovalent interactions appeared to depend upon the presence of a diammonium salt, since there was little discrimination when the nucleic acid interacted with the D- or L-amino acid alone.

Some details of the reaction reported here argue against its direct involvement in the early evolution of the chirality of nucleosides and amino acids. In particular, the presence of a N-protecting group precludes its participation in a recursive mechanism for peptide-bond formation. Moreover, we have observed that when the activated amino acid carries no N-protecting group, the selectivity is reversed, and it is the D-amino acid that is selected by D polynucleotides.[2,17] The structural features responsible for these stereochemical results are now under investigation.

Acknowledgment. We thank Professor W. H. Pirkle for the gift of a chiral HPLC column and the National Aeronautics and Space Administration (Grant NAGW-493) for financial support.

Registry No. Poly(A), 24937-83-5; poly(I), 30918-54-8; poly(U), 27416-86-0; poly(C), 30811-80-4; imidazolide of *N*-(3,5-dinitrobenzoyl)-DL-alanine, 91157-76-5.

(5) Profy, A. T.; Lo, K.-M.; Usher, D. A. *Nucleic Acids Res.* **1983**, *11*, 1617-1632.
(6) The column and the composition of the eluant were provided by Professor W. H. Pirkle.
(7) White, W. E., Jr.; Lacey, J. C., Jr.; Weber, A. L. *Biochem. Biophys. Res. Commun.* **1973**, *51*, 283-291.
(8) Weber, A. L.; Fox, S. W. *Biochim. Biophys. Acta* **1973**, *319*, 174-187.
(9) Weber, A. L.; Lacey, J. C., Jr. *J. Mol. Evol.* **1975**, *6*, 309-320.
(10) Herlinger, H.; Kleimann, H.; Ugi, I. *Justus Liebigs Ann. Chem.* **1967**, *706*, 37-46.
(11) Cervinka, O.; Budilova, J. *Collect. Czech. Chem. Commun.* **1967**, *32*, 2383-2386.
(12) (a) Doty, P.; Lundberg, R. D. *J. Am. Chem. Soc.* **1956**, *78*, 4810-4812. (b) Matsuura, K.; Inoue, S.; Tsuruta, T. *Makromol. Chem.* **1965**, *85*, 284-286. (c) Tsuruta, T.; Inoue, S.; Matsuura, K. *Biopolymers* **1967**, *5*, 313-319.
(13) Blair, N. E.; Bonner, W. A. *Origins Life* **1980**, *10*, 255-263.
(14) (a) Imanishi, Y.; Ohnishi, H.; Hashimoto, Y. *Int. J. Biol. Macromol.* **1981**, *3*, 97-104. (b) Hashimoto, Y.; Imanishi, Y. *Biopolymers* **1981**, *20*, 507-524.
(15) (a) Gabbay, E.; Kleinman, R. *J. Am. Chem. Soc.* **1967**, *89*, 7123-7125. (b) Gabbay, E. J.; Kleinman, R.; Shimshak, R. R. *Ibid.* **1968**, *90*, 1927-1928. (c) Gabbay, E. J. *Ibid.* 5257-5263. (d) Gabbay, E. J.; Kleinman, R. W. *Biochem. J.* **1970**, *117*, 247-256.
(16) Gabbay, E. J.; Kleinman, R.; Shimshak, R. R. *Biopolymers* **1968**, *6*, 993-996.
(17) Usher, D. A.; Profy, A. T.; Needels, M. C., unpublished results.

Very High 1,2-Asymmetric Induction in the Reaction of Allyl-9-BBN with Certain Imines. Evidence for a Stereoelectronic Effect To Enhance the Cram Selectivity

Yoshinori Yamamoto,* Toshiaki Komatsu, and Kazuhiro Maruyama

Department of Chemistry, Faculty of Science Kyoto University, Kyoto 606, Japan

Received April 18, 1984

The discovery of new methods for 1,2- and 1,3-asymmetric induction in acyclic systems has been of keen interest in synthetic and theoretical organic chemistry.[1] Especially, the Cram/anti-Cram problem has been one of the longstanding concerns, and unfortunately the Cram selectivity of ordinary aldehydes having an α-chiral center is generally no so high (eq 1).[2-4] We have discovered that the Cram selectivity is remarkably enhanced in the reaction of imines with allyl-9-BBN (eq 2). This finding and elucidation of the enhancement provide a conceptual advance in the Cram/anti-Cram problem.

The low Cram selectivity in the reaction of allyllic organo-

(1) For example: Heathcock, C. H. In "Comprehensive Carbanion Chemistry"; Durst, T., Buncel, E., Eds.; Elsevier: New York, 1984. Evans, D. A.; Nelson, J. V.; Taber, T. R. "Topics in Stereochemistry"; Wiley-Interscience: New York, 1982; Vol 13, p 1. "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol 2. Masamune, S. In "Organic Syntheses Today and Tomorrow"; Trost, B. M., Hutchinson, R., Eds.; Pergamon Press: New York, 1981; p 197. Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357.
(2) Excellent 1,2- and 1,3-asymmetric induction through chelation control has been realized in the nucleophilic addition of organometallics to α- and β-alkoxy substituted aldehydes. Reetz, M. T.; Kesseler, K.; Schmidtberger, S.; Wenderoth, B.; Steinbach, R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 989. Reetz, M. T.; Jung, A. *J. Am. Chem. Soc.* **1983**, *105*, 4833. Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035. Still, W. C.; McDonald, J. H. *Ibid.* **1980**, *21*, 1031.

0002-7863/84/1506-5031$01.50/0