in both cases the cells are characterized by their loss of susceptibility to contact inhibition, and by their ability to synthesize collagen, a normal function of the fibroblast which appears to be suppressed in line 3T3. These characteristics acquired by viral transformed cells appear to be due to the release of latent cellular properties.

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*THE SYNTHESIS OF COMPOUNDS POSSESSING KINETIN ACTIVITY. THE USE OF A BLOCKING GROUP AT THE 9-POSITION OF ADENINE FOR THE SYNTHESIS OF 1-SUBSTITUTED ADENINES**

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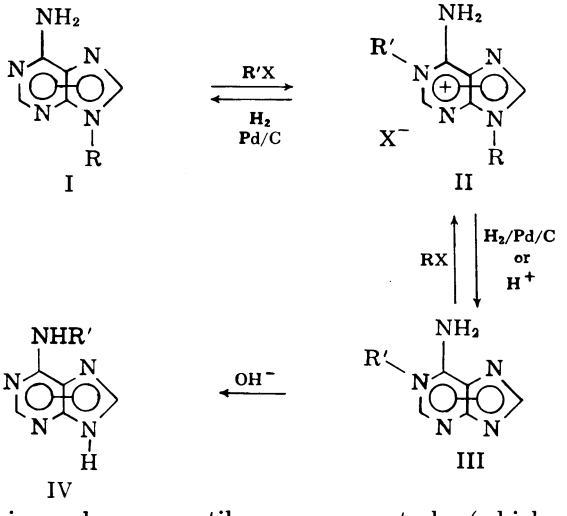
In the interest of synthesizing the remaining N-isomer of triacanthine (3-(γ,γ-dimethylallyl)-adenine),[1-6] namely, 1-(γ,γ-dimethylallyl)-adenine (type III), and other 1-substituted adenines and of studying their chemical and biological properties, we have investigated the use of a removable blocking group at the 9-position to direct an incoming substituent to the 1-position. For example, 9-benzyladenine (type I), mp 233–235°,[7-9] pK'_a *ca.* 3.2 (50% aqueous DMF), reacted with methyl iodide in dimethylacetamide to give (80% yield) 9-benzyl-1-methyladenine iodide

(Type II), mp 268–270° dec.[10] The structure was assignable by analogy with Jones and Robins' methylation of adenosine and 2′-deoxyadenosine,[11–13] by similarity of the ultraviolet spectrum ($\lambda_{max}^{H_2O}$ 259 mμ (ε 14,100), λ_{min} 243 (8,900); essentially unchanged in 0.1 *N* HCl) with that of 2′-deoxy-1-methyladenosine hydriodide,[11] and by debenzylation using hydrogen and palladium/charcoal[9, 14, 15] on the corresponding chloride (80% yield) to 1-methyladenine[11, 12] ("spongopurine"),[16] mp 297–299° dec, identified by direct comparison.[17] The *general 1-alkylation procedure* (I→II→III), of which the methylation is representative, was examined in the reverse sense. 1-Benzyladenine (type III, see below) was converted (73% yield) to 1-benzyl-9-methyladenine iodide (type II), mp 233–235° dec; $\lambda_{max}^{H_2O}$ 261 mμ (ε 13,000) and 216 (36,400); λ_{min} 245 (7,900) and 207 (34,700), which was debenzylated by conversion to the chloride and treatment with hydrogen and palladium/charcoal, yielding (71%) 9-methyladenine, mp 305–307°.[17, 18] The essentially reciprocal directivity in alkylation of the 1- and 9- substituents on adenine is parallel to that of the 3- and 7-substituents.[9] By the designations of structure which we have employed (I, II, III), we prefer not to commit ourselves as to



tautomeric forms in each case until our n.m.r. study (which will be reported separately) is complete.

The 1-benzyladenine was made by the method which Jones and Robins used for 1-methylation of adenosine and 2′-deoxyadenosine.[12] We employed benzyl bromide in dimethylacetamide at 33° followed by hydrolysis with 0.5 *N* hydrochloric acid at 90–95° for 45 min (I→II→III, 41% yield). The product, mp 244–246°, pK'_a 6.4 and 11.2 (50% aqueous DMF); hydrochloride, mp 264–265° dec, was unlike the previously known N-benzyladenine isomers (3-, 7-, 9- and 6-NH-) and had ultraviolet spectra similar to the corresponding spectra for 1-methyladenine:[11, 12] $\lambda_{max}^{H_2O}$ 265 mμ (ε 12,800), λ_{min} 241.5 (5,500); $\lambda_{max}^{0.1\ N\ HCl}$ 260.5 (13,200), λ_{min} 235 (4,100); $\lambda_{max}^{0.1\ N\ NaOH}$ 271.5 (15,000), λ_{min} 241.5 (3,500); isosbestic points 263.5 and 237.5 mμ. Final identification as 1-benzyladenine rested on its rearrangement to 6-benzylaminopurine (type IV), mp 232–234°,[8, 19–21] on refluxing with 0.2 *N* sodium hydroxide for 70 min.[11, 12, 22] 1-(γ,γ-Dimethylallyl)-adenine (type III), mp 237–239° dec, pK'_a 6.6 and 11.6 (50% aqueous DMF); hydrochloride, mp 232–233°

dec, made similarly from adenosine and γ,γ-dimethylallyl bromide, was unlike the previously known triacanthine and its isomers[1-6] and was identified by ultraviolet spectra (similar to those of 1-benzyl- and 1-methyladenine) and by conversion in refluxing alkaline solution to 6-(γ,γ-dimethylallylamino)-purine (type IV), mp 213–215° (reported 208–209°),[5] pK'_a 3.4 and 10.4 (50% aqueous DMF), which was synthesized also in this laboratory from 6-chloropurine or 6-methylmercaptopurine and γ,γ-dimethylallylamine.[23]

The 6-(γ,γ-dimethylallylamino)-purine is of special biological interest since it is *more active* than kinetin (6-furfurylaminopurine)[24, 25] in promoting the growth of tobacco tissue.[26] Results on the biological activity of the *1-substituted adenines*, e.g., 1-(γ,γ-dimethylallyl)-adenine and 1-benzyladenine, are being reported separately from the University of Wisconsin in this issue.[27] Possible conversion of 1-(γ,γ-dimethylallyl)-adenine to a 6-substituted-amino isomer by methods other than treatment with alkali is being investigated in our laboratory in order to clarify the structural basis of the kinetin activity of 1-substituted adenines.

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