set for the quantum yield for $C_2H_2D_2$ is evidence that efficient cyclobutane formation and decomposition is not taking place. The increase in cyclobutane yield with increased pressure of ethylene or inert gas indicates, however, that some collisional stabilization of vibrationally excited cyclobutane is occurring. It has been noted[8] that excited ethylene appears to undergo efficient electronic as well as vibrational energy relaxation on collision with other ethylene molecules. At 70 cm. a quantum yield of 3.8×10^{-6} for cyclobutane formation then becomes to an order of magnitude the lower limit for the collision efficiency for addition of excited ethylene to a carbon–carbon double bond. This is between the efficiencies of 1.1×10^{-3} and 3.1×10^{-9} reported[9] for the addition of hydrogen atoms and methyl radicals to ethylene at *ca.* 25°. Thus, the excited ethylene species does not appear to be exceedingly more reactive than these monoradicals in their ground states.

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DEPARTMENT OF CHEMISTRY JOHN P. CHESICK
HAVERFORD COLLEGE
HAVERFORD, PENNSYLVANIA

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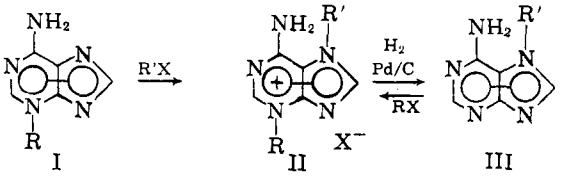
The Synthesis of 7-Substituted Adenines through the Use of a Blocking Group at the 3-Position. Site of Alkylation of 7-Substituted Adenines[1]

Sir:

The recent communication by Montgomery and Thomas[2] of the synthesis of 7-α-D-ribofuranosyladenine, the nucleoside moiety of pseudovitamin B_{12}, and its anomer, starting from 3-benzyladenine prompts us to record a direct, general synthesis which we have employed for 7-substituted adenines.[3] Treatment of adenine with benzyl,[2] allyl, and γ,γ-dimethylallyl bromide in dimethylacetamide furnished, after basification, the corresponding 3-substituted adenine (I) as the major product (55–66%): 3-benzyladenine, m.p. 278–280°[4,5], pK_a' 5.0 ± 0.1 in 50% DMF; 3-allyladenine, m.p. 204–205°, pK_a' 5.2; 3-(γ,γ-dimethylallyl)-adenine (*triacanthine*), m.p. 230–231°,[6] pK_a' 5.4.[7] *The efficient formation of the last of the group constitutes the most direct synthesis of triacanthine.*[6,8] Characterization of all as 3-substituted adenines is readily achieved by determination of their acid dissociation constants and their ultraviolet spectra in neutral and acid media.[6,8] Preferential 3-substitution on adenine[9–11] was accompanied by formation of the corresponding 9-substituted adenines (10–14%) and 1-substituted adenines (7–13%), paralleling the experience of Pal[10] in ethylation and methylation under different conditions.



The 3-substituted adenines described above underwent methylation mainly at the 7-position (II) (71–76% yield) when heated with methyl iodide in acetone or dimethylacetamide: 3-benzyl-7-methyladenine iodide, m.p. 261–262°; 3-allyl-7-methyladenine iodide, m.p. 256–258°; 3-(γ,γ-dimethylallyl)-7-methyladenine iodide (*triacanthine methiodide*),[6] m.p. 236–239°. The salts were readily converted to perchlorates or chlorides and as such had similar ultraviolet spectra (*e.g.*, 3-(γ,γ-dimethylallyl)-7-methyladenine perchlorate: $\lambda_{max}^{H_2O}$ 277 mμ (ε 17,100); λ_{sh} 223 (13,300); λ_{min} 241 (4400) essentially unchanged in 0.1 *N* HCl; $\lambda_{max}^{1.0\ N\ NaOH}$ 281 (15,800); λ_{min} 242 (2500); isosbestic point, 282 mμ) indicative of identical positional disubstitution.[12] The location of the methyl group was established by hydrogenolysis, which led in each case to the formation of some 7-methyladenine (III), m.p. 349–350° dec.,[13] produced most efficiently (72%), along with toluene, from 3-benzyl-7-methyladenine chloride. The synthesis of 7-methyladenine by benzyl blocking at the 3-position of adenine (I), followed by methylation on N-7 (II) and hydrogenolysis at N-3 (III), is only one representative of a *general 7-alkylation procedure.*

The preferred site of alkylation of 7-substituted adenines has been determined readily in the corollary experiment (III → II) of heating 7-methyladenine with benzyl, allyl, and γ,γ-dimethylallyl bromide in dimethylacetamide to yield (71–84%) the corresponding 3-benzyl-7-methyladenine bromide, m.p. 254–255°; 3-allyl-7-methyladenine bromide, m.p. 241–243°; 3-(γ,γ-dimethylallyl)-7-methyladenine bromide, m.p. 230–231°. These salts, converted to a common anion, were identical with the separate 3,7-disubstituted adenine salts produced by the first route (I → II).[14,15] Further interest in the hydrogenolytic cleavage stems from the partially selective conversion, using hydrogen and palladium/charcoal, of 3,7-dibenzyladenine chloride (obtained from the bromide, m.p. 205–207°, which was made by benzylation of 3-benzyladenine), to 7-benzyladenine, m.p. 236–238° dec.

(1) Supported by a research grant (USPHS-RG5829, currently GM-05829-05) from the National Institutes of Health, U. S. Public Health Service.

(2) J. A. Montgomery and H. J. Thomas, *J. Am. Chem. Soc.*, **85**, 2672 (1963).

(3) Reported at the Second International Symposium on the Chemistry of Natural Products, Prague, Czechoslovakia, August, 1962, and in the Reilly Lectures, University of Notre Dame, November, 1962.

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(5) We have ascertained that the material obtained according to the directions of M. Krüger, *Z. physiol. Chem.*, **18**, 423 (1894), and G. Thoiss, *ibid.*, **13**, 395 (1889), namely, treatment of adenine with benzyl chloride in the presence of potassium hydroxide, is a mixture of 3-benzyladenine and 9-benzyladenine, m.p. 233–235°.

(6) See N. J. Leonard and J. A. Deyrup, *J. Am. Chem. Soc.*, **84**, 2148 (1962), and references therein.

(7) Correct analyses have been obtained for all of the compounds reported herein.

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(11) N. J. Leonard and R. A. Laursen, *J. Am. Chem. Soc.*, **85**, 2026 (1963).

(12) Dr. R. K. Robins, Arizona State University, Tempe, Ariz., has kindly informed us of his similar results on the methylation of 3-methyladenine.

(13) We are grateful to Dr. R. K. Robins and to Dr. E. C. Taylor, Jr., of Princeton University, for providing us with authentic samples of 7-methyladenine, with which our product was identical.

(14) In the case of the 3-(γ,γ-dimethylallyl)-7-methyladenine salt, the structure of our triacanthine methiodide[6] is thus confirmed (see above and ref. 6).

(15) The n.m.r. spectra of compound types I, II, and III will be discussed fully in a forthcoming joint publication from Dr. Robins' Laboratory and our own.

THE NOYES CHEMICAL LABORATORY NELSON J. LEONARD
UNIVERSITY OF ILLINOIS TOZO FUJII
URBANA, ILLINOIS

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