responding low molecular weight amino acid active esters.

N,S-Di-Z-L-Cys-Gly-OBz was obtained by allowing IIf (1 g containing 1 mmole of cysteine) to react with glycine benzyl ester (0.5 mmole) in DMF (20 ml) with stirring for 5–8 hr at room temperature. The polymer was removed by centrifugation and washed with DMF, and the combined DMF solutions were evaporated to dryness *in vacuo*. The residue was dissolved in wet ethyl acetate and washed with 1 *N* HCl, 5% $NaHCO_3$, and water. On evaporation of the ethyl acetate a chromatographically pure solid product was obtained; yield 98%, based on the amount of glycine benzyl ester employed; mp 116–118°, $[\alpha]^{25}D$ −45.3° (*c* 1.3, DMF) [lit. mp 118–119°,[3] $[\alpha]^{25}D$ −45.5° (*c* 2.0, DMF)[3]]. Z-L-Pro-Gly-OBz was obtained analogously from IIe and glycine benzyl ester; yield 90%, mp 87–88° (lit. mp 88–89°[4]). Z-L-Ileu-(L-Ala)$_5$-PNB was obtained by coupling IId with H_2N-(L-Ala)$_5$-PNB in DMF at room temperature; yield 71%, mp 258–260°, $[\alpha]^{25}D$ −91.1° (*c* 0.34, dichloroacetic acid). An identical peptide was obtained by the DCC method; mp 261–265°, $[\alpha]^{25}D$ −90.5° (*c* 0.46, dichloroacetic acid). N,S-Di-Z-glutathione dibenzyl ester (N-Z-L-Glu-(α-OBz)-L-Cys-(-S-Z)-Gly-OBz), mp 156°, $[\alpha]^{25}D$ −35.5° (*c* 1.0, methanol) [lit. mp 158–159°,[3] $[\alpha]^{25}D$ −35.5° (*c* 1.0, methanol)[3]] was obtained in 85% yield from IIg and S-Z-L-Cys-Gly-OBz. The latter was derived from the N,S-di-Z-L-Cys-Gly-OBz preparation obtained from IIf and Gly-OBz on treatment with HBr in glacial acetic acid. Treating L-alanine *p*-nitrobenzyl ester with excess IIc, removal of the Z-group (by HBr–CH_3COOH) from the dipeptide formed (Z-L-Phe-L-Ala-PNB), neutralization with triethylamine in DMF, and treating the dipeptide ester with a new excess of IIc gave Z-L-Phe-L-Phe-L-Ala-PNB in an over-all 84% yield; mp 159°, $[\alpha]^{25}D$ −26.8° (*c* 0.9, DMF). The same peptide prepared by the DCC method gave mp 160°, $[\alpha]^{25}D$ −26.2° (*c* 1.39, DMF). Z-L-Phe-L-Phe-L-Phe-NH_2 was prepared analogously in 81% yield, mp 227°, $[\alpha]^{25}D$ −31.5° (*c* 0.8, DMF). The same peptide prepared by the DCC method gave mp 226°, $[\alpha]^{25}D$ −32.1° (*c* 1.2, DMF).

A comparison of the method for peptide synthesis described here with that of Merrifield[5] reveals that whereas in the "solid-phase peptide synthesis"[5] it is the peptide which is bound to the insoluble carrier and the N-blocked amino acid active ester is added while in solution, in our case a solution of free peptide ester is added to an insoluble N-blocked amino acid active ester. Furthermore, purification of the intermediate peptides formed during synthesis can be readily effected in our method, since these peptides are liberated into solution. In the Merrifield synthesis, on the other hand, peptide purification can be carried out only after detachment of the final product from the polymeric carrier. In the procedure described here the reaction between peptide ester and active amino acid ester can be carried out in the presence of a large excess of insoluble active ester which can be readily removed at the end of the reaction. It is thus possible to increase yields and to shorten the time of the coupling reaction.

The application of the new method for the synthesis of various low and high molecular weight peptides is under investigation.

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Synthesis of Purine Cyclonucleoside Having a 8,2′-O-Anhydro Linkage

Sir:

Synthesis of various purine cyclonucleosides containing S-anhydro linkages has been reported.[1-3] These compounds were easily desulfurized to afford 2′-deoxyadenosine, 3′-deoxyadenosine (cordycepin), and 5′-deoxyguanosine.

In analogy to similar studies[4] with pyrimidine cyclonucleosides, it would be of interest to investigate the physical and chemical properties of the purine cyclonucleosides containing O-anhydro linkages. Although an earlier attempt[5] to obtain an 8-hydroxypurine nucleoside met with little success, a novel method for the introduction of a hydroxyl group in the 8 position of preformed purine nucleoside has been developed recently in our laboratory.[6]

We wish to report the synthesis of 8,2′-anhydro-8-hydroxy-9-β-D-arabinofuranosyladenine (I), the first purine cyclonucleoside having an O-anhydro linkage. 2′,3′-O-Isopropylideneadenosine (II) was brominated by the method of Holmes, *et al.*,[7] to give 8-bromo-2′,3′-O-isopropylideneadenosine, mp 215–217° (*Anal.* Calcd for $C_{13}H_{16}O_4N_5Br$: C, 40.69; H, 4.18; N, 18.13. Found: C, 40.60; H, 4.35; N, 18.48); ultraviolet λ_{max}^{EtOH} 265 mμ, $\lambda_{max}^{H^+,\ OH^-}$ 264 mμ; R_f(A)[8] 0.60, (B) 0.73. Acetylation of this compound gave 8-bromo-2′,3′-O-isopropylidene-5′-O-acetyladenosine (III), mp 158–159° (*Anal.* Calcd for $C_{15}H_{18}O_5N_5Br$: C, 42.06; H, 4.47; N, 16.38. Found: C, 41.92; H, 4.19; N, 16.71); R_f(B) 0.82. The over-all yield of III from II was *ca.* 30%. Compound III could be obtained also from 2′,3′-O-isopropylidene-5′-O-acetyladenosine[9] by the

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(5) Condensation of 8-hydroxyadenine chloromercury salt with a protected ribosyl halide by Davoll's procedure gave only unidentified products (M. Ikahara and H. Tada, unpublished experiment).
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(7) R. E. Holmes and R. K. Robins, *J. Am. Chem. Soc.*, **86**, 1242 (1964).
(8) R_f(A) stands for the R_f value of the paper chromatography carried out by ascending technique in solvent A. Solvent A: 1-butanol–acetic acid–water, 4:1:5 (upper layer was used); solvent B: 1-butanol–water, 86:14; solvent C: solvent B–concentrated ammonia, 100:1; solvent D: water adjusted at pH 10 with ammonia; solvent E: 1-propanol–water, 3:1; solvent G: 2-propanol–concentrated ammonia–water, 7:1:2.
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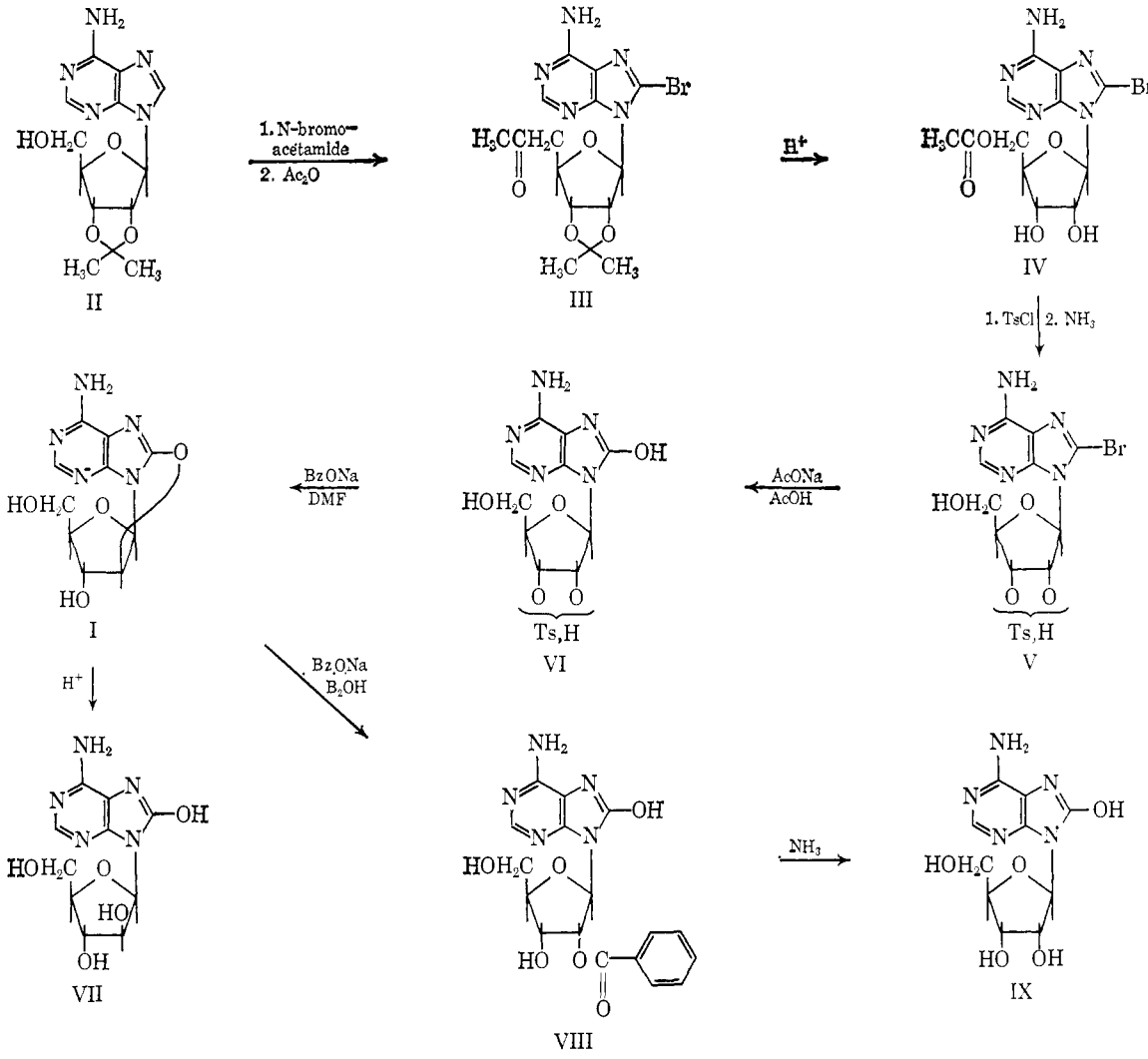

bromination reaction in 45% yield. After the isopropylidene group was removed with formic acid, the resulting 8-bromo-5′-O-acetyladenosine (IV) (glass, *Anal.* Calcd for $C_{12}H_{14}O_5N_5Br$: C, 37.12; H, 3.63; N, 18.04. Found: C, 37.20; H, 3.84; N, 18.46; R_f(C) 0.66 (D) 0.64; infrared ν_{max}^{KBr} 1740 cm^{-1} (acetate); ultraviolet λ_{max}^{EtOH} 263–264 mμ) was tosylated with 1.1 equiv of *p*-toluenesulfonyl chloride in pyridine. After deacetylation with methanolic ammonia, the resulting tosylate mixture (V) gave elemental analyses consistent with a monotosylate (*Anal.* Calcd for $C_{17}H_{18}O_6N_5BrS\cdot H_2O$: C, 39.98; H, 3.89; N, 13.51. Found: C, 39.31; H, 4.00; N, 13.47). Compound V was refluxed with sodium acetate in acetic acid[6] for 2.5 hr to give a mixture of 8-hydroxy derivatives (VI) (ultraviolet $\lambda_{max}^{H^+}$ 264 and 283 mμ, $\lambda_{max}^{OH^-}$ 279 mμ; infrared ν_{max}^{KBr} 1715 cm^{-1} (8-CO)), which was heated at 100–105° with sodium benzoate in DMF for 2 hr. Purification of the mixture by column chromatography on cellulose powder gave a crystalline compound (I) (R_f(C) 0.14, (D) 0.47), which darkened at 190° and decomposed at 210°. Ultraviolet absorption properties of I ($\lambda_{max}^{H_2O}$ 260 mμ (ε 11.0 × 10^3), $\lambda_{max}^{pH\ 1}$ 260 mμ (ε 10.8 × 10^3), $\lambda_{max}^{pH\ 14}$ 260 mμ (ε 10.7 × 10^3)) closely resembled those reported for 8-methoxyadenosine.[10] Evidence indicating the 8,2′-anhydro structure of I derives from the following observation: the infrared spectra of I (KBr disk) shows loss of the band at 1715 cm^{-1}. Compound I shows a high negative rotation, $[\alpha]^{19}D$ −121.6° (*c* 0.75, pyridine),[1] and gives an elemental analysis for $C_{10}H_{11}O_4N_5$: C, 45.28; H, 4.18; N, 26.41. Found: C, 45.08; H, 4.74; N, 26.94. An analogous reaction for the formation of anhydronucleosides by reaction of sulfonyloxy derivatives of pyrimidine with sodium benzoate in DMF has already been reported.[11] Further evidence for the 8,2′-anhydro structure was obtained by refluxing I in 0.1 *N* sulfuric acid for 2 hr to yield the known[12] 8-hydroxyadenine (R_f(D) 0.31), an 8-hydroxy-9-glycosyladenine (VII) ($\lambda_{max}^{H^+}$ 263 and 281 mμ, $\lambda_{max}^{OH^-}$ 278 mμ), and an unidentified sugar. Compound VII differed in its chromatographic behavior in three solvent systems as shown in Table I, especially in the solvent system containing borate, from 8-hydroxy-9-β-D-xylofuranosyladenine synthesized by another procedure.[13] Since compound I does not consume periodate, whereas IX does, it must be concluded that I is 8,2′-anhydro-8-hydroxy-9-β-D-arabinofuranosyladenine. Furthermore, treatment of I with sodium benzoate in DMF in the presence of benzoic acid[11] gave 8-hydroxy-9-(2′-O-benzoyl-β-D-ribofuranosyl)adenine (VIII) (ultraviolet $\lambda_{max}^{H_2O}$ 270 mμ; $\lambda_{max}^{H^+}$ 264, 282 mμ; $\lambda_{max}^{OH^-}$ 279 mμ), which after treatment with ammonia yielded the known[10]

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Table I. R_f values of 8-Hydroxyadenine Pentofuranosides

Solvent	8-Hydroxy-adenosine	9-β-D-Arabino-furanosyl-8-hydroxy-adenine	9-β-D-Xylo-furanosyl-8-hydroxyadenine
A	0.48	0.39	0.48
B	0.23	0.14	0.24
F	0.50	0.41	0.50
G	0.43	0.27	0.37

8-hydroxyadenosine (IX), which consumed rapidly 1 mole of periodate per mole. In spite of the careful examination of the reaction mixture of the cyclization, no 8,3′-anhydro isomer is isolated. Although the reason is not elucidated as yet, large steric distortion required for the formation of 8,3′-cyclonucleoside[3] may inhibit the cyclization.

The synthesis and study of O-anhydro derivatives of other purine nucleosides are currently under investigation in this laboratory.

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The Irradiation of 1,1-Dichloro-2-phenylcyclopropane in Olefins. A Light-Induced Transfer of Dichlorocarbene[1]

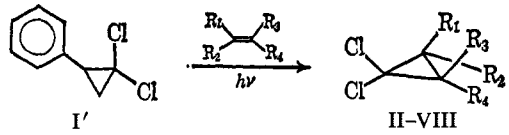
Sir:

Irradiation of solutions of 1,1-dichloro-2-phenylcyclopropane[2] (I) in olefins with light of $\lambda \geq 210$ mμ leads to rapid destruction of starting material and

Table I. Yields of 1,1-Dichlorocyclopropanes

Olefin	Product	Yield, %
cis-2-Butene	II	10
trans-2-Butene	III	9
cis-4-Methyl-2-pentene	IV	14
trans-4-Methyl-2-pentene	V	15
trans-2,5-Dimethyl-3-hexene	VI	12
2,3-Dimethyl-2-butene	VII	13
Cyclohexene	VIII	14

evolution of a mixture of products. Formally, at least, the major product of the reaction is derived from the addition of dichlorocarbene to the solvent olefin.



I′ II–VIII

II, $R_1 = R_3 = CH_3$; $R_2 = R_4 = H$
III, $R_1 = R_4 = CH_3$; $R_2 = R_3 = H$
IV, $R_1 = CH_3$; $R_3 = HC(CH_3)_2$; $R_2 = R_4 = H$
V, $R_1 = CH_3$; $R_4 = HC(CH_3)_2$; $R_2 = R_3 = H$
VI, $R_1 = R_4 = HC(CH_3)_2$; $R_2 = R_3 = H$
VII, $R_1 = R_2 = R_3 = R_4 = CH_3$
VIII, $R_1, R_3 = -CH_2CH_2CH_2CH_2-$; $R_2 = R_4 = H$

The 1,1-dichlorocyclopropanes are formed in 9–15% yield (Table I). Irradiation of dilute solutions of I in olefins was carried out using as light source a Hanovia type L 450-w high-pressure mercury arc filtered by a Vycor sleeve. Products were identified by comparison of their infrared spectra with those of authentic samples. New compounds (IV–VI) were identified by elemental analysis and comparison of their infrared spectra with those of samples prepared by the method of Doering[3] or Robinson.[4] Examination of the nuclear magnetic resonance spectra of the new compounds revealed no signals in the region expected of vinyl hydrogen[5] or hydrogen bound to carbon bearing two chlorine atoms.[6]

The decomposition of I is akin to two other reactions recently discovered. Dvoretzky and co-workers[7] have reported the photochemical cleavage of a number of arylcyclopropanes to arenes and methylene. Griffin and Kristinsson[8,9] have uncovered the photochemical extrusion of phenylcarbenes from phenyloxiranes. Both these reactions are thought to go through carbenes. There is evidence that a carbene may be the reactive intermediate in the photochemical decomposition of I as well. Irradiation of I in *cis*-2-butene produces 10% of II but less than 0.5% (probably less than 0.1%) of III. The addition appears to proceed in a *cis* fashion. Halocarbenes, or at least the species produced in the base-catalyzed decomposition of haloforms, are known to add to olefins in this manner.[10,11] Further, dichlorocarbene is known to be a powerful electrophile.[12,13] When allowed to react with pairs of olefins, dichlorocarbene chooses the more substituted. The species formed in the photolysis of I bears a strong similarity to dichlorocarbene in this respect, adding to cyclohexene a little faster than to *cis*-4-methyl-2-pentene and preferring 2,3-dimethyl-2-butene to *cis*-4-methyl-2-pentene by a factor of *ca.* 100 (Table II).

Table II

Olefin pair	$:CCl_2$ Source	Products[a]
2,3-Dimethyl-2-butene/*cis*-4-methyl-2-pentene	$CHCl_3$[b]	VII/IV = 110
2,3-Dimethyl-2-butene/*cis*-4-methyl-2-pentene	I	VII/IV = >100
Cyclohexene/*cis*-4-methyl-2-pentene	$CHCl_3$[b]	VIII/IV = 1.81
Cyclohexene/*cis*-4-methyl-2-pentene	I	VIII/IV = 2.24

[a] Corrected for varying sensitivities on gas–liquid partition chromatography. [b] Measured at −80°; $K^+{}^-OC(CH_3)_3$ as base.

These data suggest that the intermediate formed in the photolysis of I is very similar to dichlorocarbene both in its mode of addition and its electron-seeking demands. Moreover, the energy provided by the light used, *ca.* 135 kcal/mole, is adequate to break the

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