Table I. The Reaction of the *B*-Alkylboracyclanes with α,β-Unsaturated Carbonyl Derivatives

| Alkyl group of *B*-alkyl-boracyclane | α,β-Unsaturated carbonyl derivative[a] | Product[b] | Yield,[c] % | | |
|---|---|---|---|---|---|
| | | | 3,5-DMB-6[d] | 3,6-DMB-7[e] | Borinane[f] |
| *sec*-Butyl | MVK | 5-Methyl-2-heptanone | 83 (75)[g] | 80 | 74 (67)[6] |
| Cyclopentyl | MVK | 4-Cyclopentyl-2-butanone | 78 | 65 | 66 |
| Cyclohexyl | MVK | 4-Cyclohexyl-2-butanone | 81 | 74 | 80 |
| Cyclohexyl | EA | 4-Cyclohexyl-2-pentanone | 71 | | |
| *trans*-2-Methyl-cyclohexyl | MVK | 4-(2′-Methylcyclo-hexyl)-2-butanone[h] | 79 (73)[g] | | |
| *exo*-Norbornyl | MVK | 4-Norbornyl-2-butanone[i] | 81 | 61 | 65 |
| *tert*-Butyl | MVK | 5,5-Dimethyl-2-hexanone | 90 (76)[g] | | |
| *tert*-Butyl | CH | 3-(*tert*-Butyl)-cyclohexanone | 73 | | |
| 2,3-Dimethyl-2-butyl | MVK | 5,5,6-Trimethyl-2-heptanone | 88 (81)[g] | 51 | 75 (71)[g] |
| *n*-Hexyl | MVK | 2-Decanone[j] | 32 | 51 | |

[a] MVK, methyl vinyl ketone; EA, ethylideneacetone; CH, 2-cyclohexenone. [b] All products were either compared with authentic samples or exhibited spectral data in accordance with the assigned structures. All new products yielded the correct elemental analyses. [c] By glpc. Based on the olefin or alkyllithium used. [d] Using *B*-alkyl-3,5-DMB-6. [e] Using *B*-alkyl-4,6-DMB-7. [f] Using *B*-alkylborinane. [g] Numbers in parentheses are isolated yields. [h] See ref 9. [i] A single compound by glpc. Presumably the exo isomer. [j] Contaminated with 3% of an isomeric product.

The yield of a desired product is usually higher when the corresponding *B*-alkyl-3,5-DMB-6 is employed (Table I). However, this advantage may be somewhat offset, at present, by the higher cost of the starting diene, 2,4-dimethyl-1,4-pentadiene. In any event, it is evident that the present development extends the 1,4-addition reaction to hindered secondary and tertiary alkyl groups, simultaneously providing a substantial improvement in the yields of the desired products based on the starting olefins or alkyllithium compounds. Although the latter advantage of the present procedure does not extend to primary alkyl groups, this procedure does have the advantage of yielding purer products, with only small amounts of the minor isomer. For example, in the case of 1-hexene, the isomeric purity of the product is much higher (97%) than the earlier figure of 85% realized in the reaction of trialkylboranes from 1-butene and 1-octene with methyl vinyl ketone.[1a]

Isolation of the desired products offered no difficulty. Simple distillation of the reaction mixture was usually sufficient. In cases in which the *B*-hydroxyboracyclanes interfered with the distillation, this difficulty could be avoided by oxidation of the product with 30% hydrogen peroxide and 3 *N* sodium hydroxide prior to distillation.

The following procedure for the preparation of 5,5,6-trimethyl-2-heptanone from 2,3-dimethyl-2-butene is representative. *B*-Thexyl-3,5-DMB-6 was prepared as reported previously[8] by the addition of 3.36 g (40 mmol) of 2,3-dimethyl-2-butene to 25 ml (25 mmol) of a 1 *M* solution of bis(3,5-dimethyl)borinane in THF. After destroying the residual hydride with 1.8 ml (100 mmol) of water, 4.2 g (60 mmol) of methyl vinyl ketone and 2.26 g (10 mmol) of *n*-hexadecane (internal standard) were added and the reaction mixture was stirred overnight at 25°. Glpc examination of the reaction mixture indicated the presence of 35.2 mmol (88% based on 2,3-dimethyl-2-butene) of 5,5,6-trimethyl-2-heptanone. The reaction mixture was oxidized with 20 ml each of 3 *N* sodium hydroxide and 30% hydrogen peroxide in order to destroy *B*-hydroxy-3,5-DMB-6. The aqueous layer was saturated with sodium chloride. The organic layer was separated and the aqueous layer was extracted with pentane. After drying over magnesium sulfate, the combined organic layer was distilled to yield 5.05 g (81%) of 5,5,6-trimethyl-2-heptanone: bp 95–97° (20 mm); $n^{20}\text{D}$ 1.4356; ir (neat) 1720 cm$^{-1}$; pmr ($CCl_4$, TMS) δ 0.8 and 0.9 (12 H), 1.2–1.7 (m, 3 H), 1.9–2.5 (m, 5 H). *Anal.* Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 77.02; H, 12.97.

In view of the fact that an increasing number of reactions of organoboranes involve free-radical mechanisms, it seems likely that application of the presently described *B*-alkylboracyclanes in such reactions, in place of simple trialkylboranes, will provide improvements similar to the present results.[11]

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(11) H. C. Brown and M. M. Midland, *J. Amer. Chem. Soc.*, **93**, 3291 (1971).

(12) Postdoctoral Research Associate on Grant No. DA 31-124 ARO(D) 453, supported by the U. S. Army Research Office (Durham).

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## A New Photoproduct of Cytosine. Structure and Mechanism Studies[1,2]

*Sir:*

We have characterized derivatives of a homoadduct of cytosine isolated from the irradiation (254 nm) of

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(2) This investigation was supported in part by Contract No. AT-(30-1)-2798 of the U. S. Atomic Energy Commission, and by a Public Health Service Research Career Development Award (K3-GM-4134) from NIGMS.

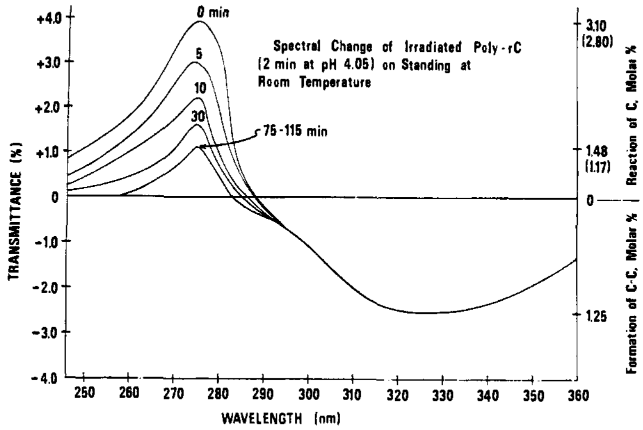

Figure 1. Difference transmittancy spectra of a 2-min irradiated poly-rC on standing at room temperature at pH 4. [The numbers given in parentheses are those corrected values in considering possible hypochromism occurring in polynucleotides.]

polycytidylic acid (poly-rC), deoxycytidine (CdR), and cytidine (CR). This adduct should be of importance in the photobiology of nucleic acids because it forms in major proportion (26%)[3] in poly-rC irradiated with biological uv doses and its stability may cause permanent effects. There are indications that these photoadducts are formed in poly(dG·dC) and in naturally occurring DNA (unpublished results). Furthermore, the solution pH dramatically influences the photoadduct yields. Also, these photoadducts are possibly produced through charge-transfer complexes. The latter two observations should be of general interest in photochemistry.

Irradiation of poly-rC in water and in pH 7 phosphate and pH 4 acetate-buffered solutions results in absorbancy decreases (or transmittancy (T) increases) in the 275-nm region with concomitant increases in the 330-nm region, as shown in Figure 1. When a 2-min irradiated ($5 \times 10^6$ ergs/ml) poly-rC solution ($OD_{274}$ 0.76, pH 4, double helices)[4] was allowed to stand at room temperature, the decrease in $T_{329}$ remained unchanged, while the increase in $T_{274}$ decayed to a stationary state in ~75 min.[3]

Paper chromatographic separation of the 329-nm absorbing compound ($R_f$ 0.50, eluent 0.1 *N* HCl) from the acid hydrolysates of irradiated poly-rC solution (water, pH 6.2) yielded sufficient material to determine the uv and ir spectra. Structural elucidation with material isolated from poly-rC would be ideal but impractical. Also, various attempts showed that the irradiation of cytosine is not as promising as that of CdR and CR.

Apparently, the solution pH plays a critical role in these bimolecular photoreactions in frozen aqueous solutions.[5] As shown in Figure 2, the dramatic effect on the yield ($OD_{325}$ increase) of the formation of CdR–CdR (deaminated deoxycytidine adduct) was noted.

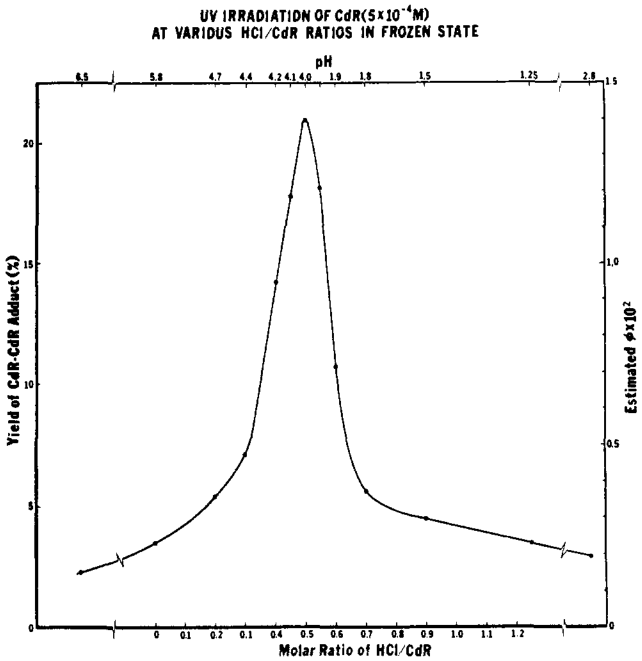

Figure 2. Yields and quantum yields of CdR–CdR from CdR irradiated in frozen state at various pH or molar ratios of HCl–CdR.

A similar pH effect was observed with the formation of CR–CR, for which the maximal yield is at pH 3.8. In both cases, the pH for the maximal yields are calculated to be 0.5 mol equiv in HCl. On the basis of the above information, yields of 15% of CR–CR and 18% of CdR–CdR were obtained from CR–0.5HCl and CdR–0.5HCl, respectively.

According to the molecular aggregation–puddle formation hypothesis,[5–7] the irradiation of frozen solutions compares to that of solid state or concentrated puddles depending on the absence or presence of low melting point organic solvent or electrolytes, respectively. In electrolyte (NaCl) puddles the adduct yields were 4% as compared with 9% in the absence of puddle effects. No adduct formation was detected after irradiation of "methanol puddles." These results suggest that adduct formation is greatly favored in the "solid" state.

Hydrolysis of CdR–CdR in trifluoroacetic acid yielded 95% deaminated cytosine–cytosine adduct (C–C). A quantitative yield of C–C was obtained from CR–CR hydrolyzed in 70% $HClO_4$. The ir spectra of C–C from these two sources and from irradiated poly-rC were identical.

The mass spectrum determined for the C–C adduct after silylation with Regisil No. 27002 in pyridine gave a molecular ion peak at *m/e* 421 corresponding to a tritrimethylsilyl derivative of a dimeric cytosine minus one molecule of ammonia. The ultraviolet spectra indicate that these compounds have the same chromophores as substituted pyrimidinones and are similar to the dehydrated adducts of uracil–uracil,[8] uracil–thymine,[9] and thymine–thymine.[10] However, the nmr spectra of these compounds (Figure 3) distinguish them from these previously known adducts. Importantly,

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(3) The reversible spectral change is generally recognized as "cytosine photohydrate" [E. Fahr, *Angew. Chem.*, 8, 578 (1969); G. DeBoer and H. E. Johns, *Biochim. Biophys. Acta*, 204, 18 (1970)]. Since this "photohydrate" is reversible and the adduct formation is irreversible, the two kinds of changes can be easily estimated. With the known values of $\epsilon_{275}$ and $\epsilon_{329}$ of the adducts, it was found that 2.87 mol % of C reacted, 1.25 mol % of C–C formed, and 1.62 mol % of "photohydrate" resulted. Thus, under the experimental conditions, 26% of the photoproducts is C–C and 38% is the "photohydrates." A third product(s), with no uv absorption maximum, accounts for the other 38%.

(4) E. O. Akinrimisi, C. Sander, and P. O. P. Ts'o, *Biochemistry*, 2, 340 (1963).

(5) S. Y. Wang, *Nature (London)*, 190, 690 (1961).

(6) S. Y. Wang, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, 24, S-71 (1965).

(7) T. C. Bruice and A. R. Butler, *ibid.*, 24, S-45 (1965).

(8) M. N. Khattak and S. Y. Wang, *Science*, 163, 1341 (1969).

(9) D. F. Rhoades and S. Y. Wang, *Biochemistry*, 9, 4416 (1970).

(10) A. J. Varghese and S. Y. Wang, *Science*, 160, 186 (1968).

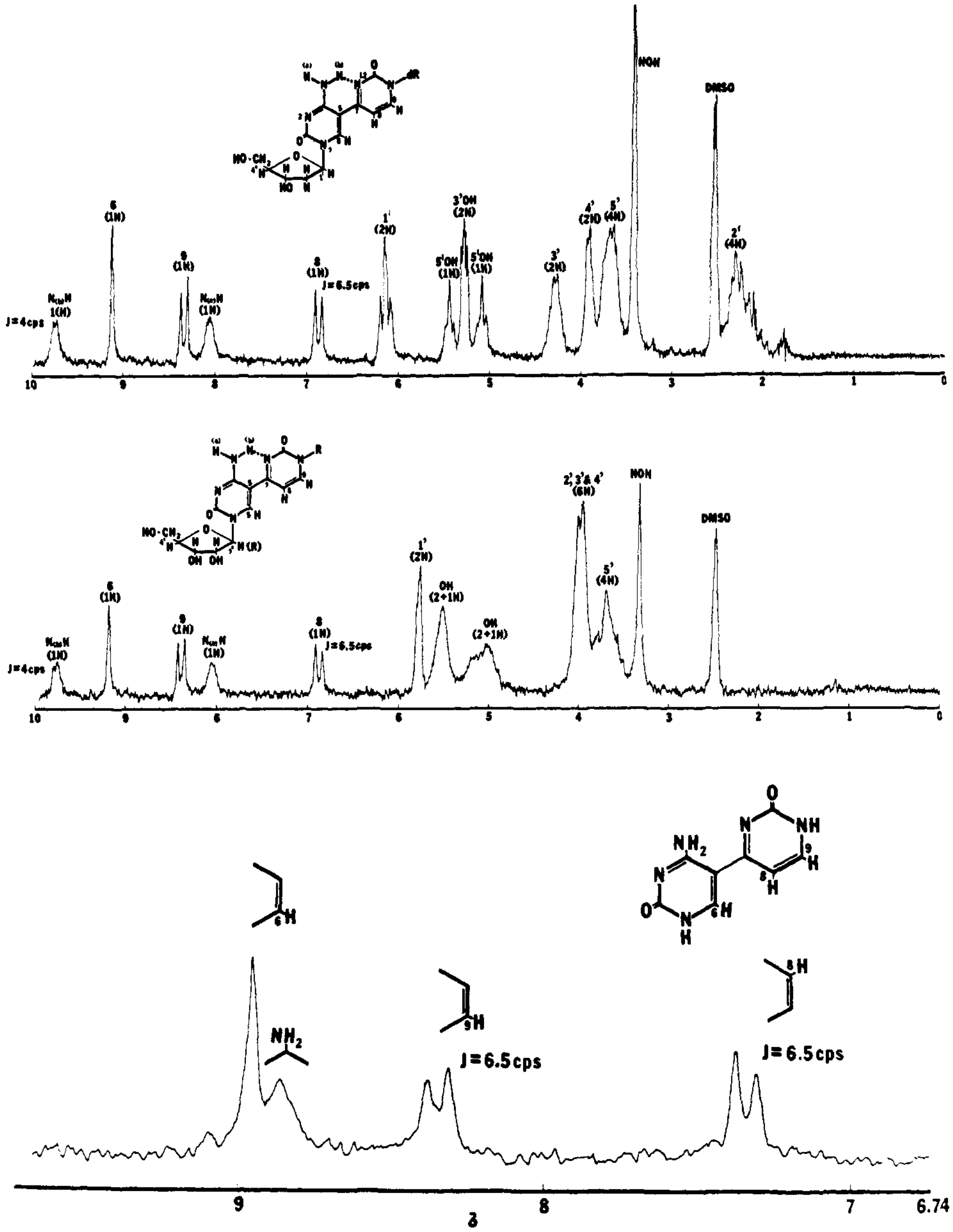

Figure 3. Nuclear magnetic resonance spectra of CdR-CdR (top) and CR-CR in $(CD_3)_2SO$ and C-C (bottom) in $CF_3COOH$ at 100 MHz with internal standard tetramethylsilane. [For clarity the numbering system used in nmr differs from that used in the naming of these compounds.]

each shows three vinyl proton signals. The pair of doublets are for C(8) and C(9). The appearance of the singlets at a low field ($\delta \sim 9$) suggests that they may be characteristic of C(6)-H[11] and that the pyrimidinone ring may be substituted at C(5). Interestingly, the two pairs of nonequivalent amino proton signals have markedly different chemical shifts ($\delta$ 8.05, 9.74 and 8.04, 9.76) indicating intramolecular H bonding. The low-field signal is most likely the one forming an H bond with N(12). Again, this favors substitution at C(5). If substitution is at C(6), such H bonding is unlikely. We may conclude that CdR-CdR is a 1,1'-bis(2'-deoxy-β-D-erythropentofuranosyl) and CR-CR is a 1,1'-di-β-D-ribofuranosyl derivative of C-C which is 4'-amino[4,5'-bipyrimidine]-2,2'(1*H*,1'*H*)-dione.

Thus, the formation of C-C in poly-rC is similar to that in frozen or solid state irradiation of CdR·0.5-HCl or CR·0.5HCl and is probably *via* the rearrangement of an azetidine intermediate. The former cases are the results of polymeric structure and the latter requires one CR and one CR-H+ for this bimolecular photoreaction to occur. Our results may support the recent finding[12] that charge-transfer interactions occur between CR and CR-H+ in stacked structures. However, this reaction is distinct in various aspects from other acid-catalyzed bimolecular photoadditions.[13]

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(11) E. D. Becker, H. T. Miles, and R. B. Bradley, *J. Amer. Chem. Soc.*, **87**, 5575 (1965).

(12) T. Montenay-Garestier and C. Hélène, *Biochemistry*, **9**, 2865 (1970).

(13) H. J. F. Angus and D. Bryce-Smith, *J. Chem. Soc.*, 4791 (1960); P. J. Kropp, *J. Amer. Chem. Soc.*, **91**, 5783 (1969); M. Kawanisi and H. Sato, *Tetrahedron Lett.*, 721 (1970); D. Bryce-Smith, R. Deshapande, A. Gilbert, and J. Grozonka, *Chem. Commun.*, 560 (1971); A. Yoshino, M. Ohashi, and T. Yonezawa, *ibid.*, 97 (1971).

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