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(19) Complex formation by the pyridine ligands in **1** involves rotation of the plane of the pyridine rings through 180°. This is seen in the upfield shift of the 2′-H and the downfield shift of the 4′-, 5′-, 6′-H's ($\Delta\delta$ −1.95, 0.03, 0.33, 0.35 ppm, respectively, compared with those of nicotinamide) in the ^1H NMR spectrum of **2c** (Me_2SO-d_6).
(20) Anal. Calcd for $C_{68}H_{44}N_{12}O_4Cu \cdot CHCl_3$ (**2b**): C, 64.94; H, 3.55; N, 13.17. Found: C, 65.01; H, 3.89. N, 13.02. M^+ is 1156.
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(23) Isosbestic points were maintained during the titration of $[(N_4)\text{-}Fe(P)]_2O$ with $CuCl_2$ solution in MeOH (512, 541 nm); an isosbestic point was also observed during the titration of $[Fe(TPP)]_2O$ with $CuCl_2$ solution in MeOH (550 mm) to give Fe(TPP)Cl.
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Photoinduced Coupling Reaction of 5-Bromouridine to Tryptophan Derivatives[1]

Sir:

The replacement of thymine in DNA by 5-bromouracil sensitizes bacterial and mammalian cells to the lethal effects of UV light.[2] The photochemical mechanism responsible for this sensitizing effect has been studied extensively, and at least three possible mechanisms have been suggested: (1) self-coupling of two 5-bromouracil residues with formation of 5–5′-diuracilyl linkages;[3] (2) induction of single-strand breaks in DNA;[2b,4] (3) enhancement in the rate of production of DNA–protein cross-links in cells.[5] Recently, DNA substituted with bromouracil has been reported to undergo photoinduced cross-linking to RNA polymerase[6] and to *lac* repressor.[6,7] In spite of the importance of the cross-linking of DNA containing 5-bromouracil to proteins,[8] very little is known about the nature

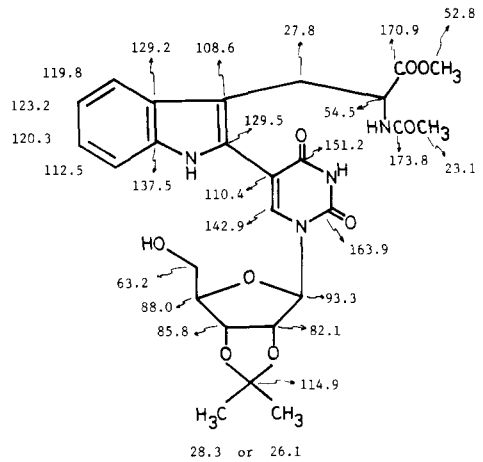
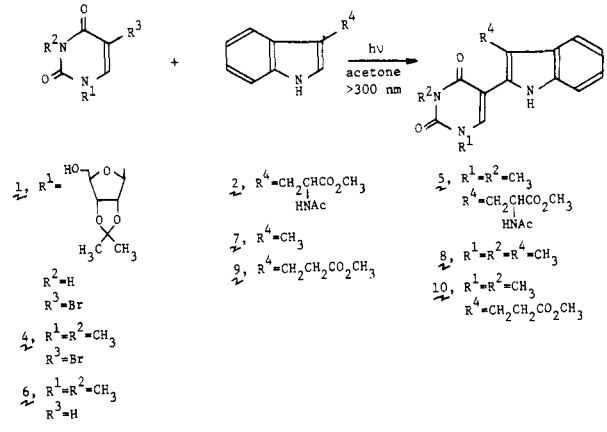


Figure 1. Structure of **3** as determined by ^{13}C NMR in Me_2CO-d_6. Chemical shifts are in parts per million from Me_4Si.

of the amino acid–nucleic acid adducts. Sulfhydryl compounds such as cysteine and glutathione have been reported to undergo photoaddition with 5-bromouracil.[9] We now wish to report that N^b-acetyltryptophan methyl ester, a model for tryptophan in a protein, undergoes a photoreaction with 5-bromouridine or 5-bromo-1,3-dimethyluracil to give the corresponding coupled product in a highly regiospecific fashion.[10] Neither *N*-acetyltyrosine methyl ester nor *N*-acetylhistidine methyl ester undergoes such a coupling reaction.

Acetone-sensitized irradiation[12] of 2′,3′,*O*-isopropylidene-5-bromouridine (**1**, 1.4 mM) in acetone–acetonitrile (1:3) in the presence of N^b-acetyltryptophan methyl ester (**2**, 3.5 mM) produced a single photoproduct. No other products, except the unreacted starting materials **1** and **2**, were detected on TLC. Separation by column chromatography on silica gel yielded **3**, mp 158–162 °C dec, in 70% yield. Spectral properties,[13] including the ^{13}C NMR spectrum[14] (Figure 1), are in accordance with the assigned structure.

Under similar conditions, acetone-sensitized irradiation[12] of 5-bromo-1,3-dimethyluracil (**4**, 1.5 mM) and **2** (3.5 mM) in acetonitrile gave rise to the coupled product **5**[15] (67%) as the sole product.[16] Quantum yield for the formation of **5** is 0.018.[17] In control runs, irradiation of a solution of **4** and **2** in acetonitrile in the absence of acetone did not produce **5**, and both starting materials were recovered unchanged. Direct irradiation of **4** (2.0 mM) and **2** (4.6 mM) in acetonitrile with 254-nm light resulted in the formation of the debrominated product 1,3-dimethyluracil (**6**, 75%) as the major product, together with minor amounts of **5** (15%).[19] Addition of 1,3-pentadiene to the system inhibited the formation of the coupled product **5**, but had no significant effect on the formation of **6**. The bromouracil derivative **4** undergoes regiospecific coupling reaction with various indolic compounds. For example, ace-



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tone-sensitized irradiation of **4** in the presence of 3-methylindole (**7**) gave **8**[20] (66%), whereas direct irradiation of **4** and methyl indole-3-propionate (**9**) with 254-nm light resulted in the formation of **6** (60%) and **10**[21] (15%).

Electrophilic substitution[22] usually occurs predominantly at the 3 position of indoles, whereas radical reactions,[23] including several photoinduced reactions,[24] proceed less selectively to give mixture of 1-, 2-, 3-, 4-, and 6-substituted indoles. In the present case, however, the coupling reactions occurred exclusively on the 2 position of the indole molecules. The benzenoid ring was not attacked. Such a preferential attack on the 2 position has been observed in certain photoadditions[25] or in anodic cyanation,[26] where an electron-transfer process is believed to be involved.[27]

Under conditions in which **1** reacted smoothly with **2**, both **1** and **4** were photochemically inert toward derivatives of other aromatic amino acids such as *N*-acetylhistidine methyl ester or *N*-acetyltyrosine methyl ester. Thus, the photochemical coupling reaction is *specific for tryptophan.* A similar coupling may take place between bromouracil-substituted DNA and tryptophyl residues in a protein. Thus, the coupling reactions reported here may serve as a useful model for the study of the lethal effects of UV light on cells. Moreover, because of its high selectivity, regiospecificity, and efficiency, the present reaction constitutes a useful synthetic method for the introduction of indolyl groups into the 5 position of uracil or uridine. Mechanistic aspects and other synthetic applications of this new type of photochemical coupling reactions are under study.

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(12) Irradiation was done with a 100-W high-pressure mercury lamp using a glass filter (>300 nm) at ambient temperature.
(13) UV (acetonitrile) 260 nm (log ϵ 4.07), 328 (3.72); ^{1}H NMR (Me_2CO-d_6) δ 1.35 (s, 3 H), 1.55 (s, 3 H), 1.78 (s, 3 H), 3.24 (d, 2 H, J = 8 Hz), 3.59 (s, 3 H), 3.83 (d, 2 H, J = 6 Hz), 3.76–4.13 (2 H, NH and OH), 4.25 (td, 1 H, J = 6.0, 3.0 Hz), 4.78 (td, 1 H, J = 8.0, 8.0 Hz), 4.98 (dd, 1 H, J = 14.0, 2.4 Hz), 5.02 (dd, 1 H, J = 14.0, 3.0 Hz), 6.12 (d, 1 H, J = 2.4 Hz), 6.95–7.64 (m, 4 H), 7.69 (br d, 1 H, J = 8.0 Hz, NH), 8.22 (s, 1 H), 10.25 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 542.20036 (M^+) (calcd for $C_{26}H_{30}N_4O_9$, 542.20124).
(14) Assignments are based on multiplicities in the off-resonance decoupled spectrum and on chemical shifts in model compounds.
(15) Mp 222–224 °C dec; UV (acetonitrile) 264 nm (log ϵ 4.08), 288 (4.02), 337 (3.73); ^{1}H NMR ($CDCl_3$ δ 1.96 (s, 3 H), 3.32 (d, 2 H, J = 8 Hz), 3.36 (s, 3 H), 3.44 (s, 3 H), 3.62 (s, 3 H), 4.71 (td, 1 H, J = 8.0, 8.0 Hz), 6.64 (d, 1 H, J = 8 Hz, NH), 7.03–7.54 (m, 4 H), 8.09 (s, 1 H), 10.29 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 398.1592 (M^+) (calcd for $C_{20}H_{22}N_4O_5$, 398.1590).
(16) Essentially the same result has been obtained in aqueous acetone.
(17) Quantum-yield measurement was carried out at 20 °C using benzophenone–benzhydrol actinometry.[18] Potassium chromate in an aqueous solution of potassium carbonate was used to isolate the 313-nm region of the high-pressure mercury arc.
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(20) Mp 198–201 °C; UV (acetonitrile) 260 nm (log ϵ 3.95), 291 (3.98), 340 (3.72); ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 3 H), 3.35 (s, 3 H), 3.38 (s, 3 H), 6.96–7.58 (m, 4 H), 7.94 (s, 1 H), 9.92 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 269.1142 (M^+) (calcd for $C_{15}H_{15}N_3O_2$, 269.1164).
(21) Mp 59–60 °C; UV (acetonitrile) 264 (log ϵ 4.00), 282 (4.01), 332 (3.74); ^{1}H NMR ($CDCl_3$) δ 2.67–3.32 (m, 4 H), 3.45 (s, 3 H), 3.57 (s, 3 H), 3.67 (s, 3 H), 7.01–7.66 (m, 4 H), 8.07 (s, 1 H), 9.87 (br s, 1 H, NH); mass spectrum (high resolution) *m/e* 341.1354 (M^+) (calcd for $C_{18}H_{19}N_3O_4$, 341.1374).
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Gas Phase Photodissociation of $C_7H_7^+$

Sir:

The $C_7H_7^+$ cation continues to present a challenging structural problem to mass spectroscopists. Extensive mass spectroscopic[1-4] and ion photodissociation[5] results using specifically labeled precursors (^{2}H, ^{13}C) show that hydrogen and carbon scrambling occur to a large degree in the formation and fragmentation of $C_7H_7^+$. Such results are suggestive of the symmetrical tropylium ion (I). On the other hand, ions having

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enough internal energy to fragment will undoubtedly undergo molecular rearrangement prior to dissociation and therefore may not reflect the ground state structure or stability of the ion. Studies utilizing collisional activation (CA) or collision induced dissociation (CID) techniques, generally believed to yield ground-state structural information, have indicated that $C_7H_7^+$ obtained from toluene, for example, is a mixture of isomers possibly undergoing interconversion.[6] These techniques, however, by their very nature may also promote scrambling prior to dissociation and detection and, in addition, sample ions that may have lifetimes only on the order of 10^{-5} s.

The most convincing evidence for the long-lived existence of more than one cyclic isomer of $C_7H_7^+$ in the gas phase comes from ion–molecule reaction studies using ion cyclotron resonance (ICR) spectroscopy.[7-9] Shen et al.[7] concluded from

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