ammonia and 10 mL of water. The solution on cooling deposited 1.8 g (87%) of colorless crystals of the imine G (RR = $(CH_2)_5$): mp 294–295 °C, raised by recrystallization from ethanol–water to 300–301 °C; IR 1700 (C=O), 1670 (C=N) cm^{-1}; NMR (TFA) δ 0.6–1.7 (m, 14 H), 7.7 (s, 1 H, NH), 8.7 (s, 1 H, NH), 9.0 (s, 1 H, NH).

Anal. Calcd for $C_8H_{13}N_3O \cdot 0.5EtOH$: C, 56.83; H, 8.48. Found: C, 56.52; H, 8.45.

The same compound was isolated from a reaction mixture from which 5,5-pentamethylene-4-thiohydantoin (**5**, RR = $(CH_2)_5$) had been isolated in 49% yield, following the procedure of Carrington et al.[4] The acidic filtrate was made basic with concentrated aqueous ammonia, and a 14% yield of G (RR = $(CH_2)_5$) was obtained.

5′-Iminospiro(adamantane-2,4′-imidazolidin)-2′-one (G, RR = $C_{10}H_{14}$). The 4-thiohydantoin **5** (RR = $C_{10}H_{14}$) (2.0 g) was heated at 80–90 °C under reflux with 20 mL of concentrated ammonia, 20 mL of water, and 20 mL of ethanol for 3 h with stirring. The mixture was cooled and filtered, and the solid residue was washed with water and then extracted with dilute hydrochloric acid. The acidic solution was made basic with ammonia and 1.04 g (56%) of colorless crystals of the imine (G, RR = $C_{10}H_{14}$) separated: mp 327 °C (eff); IR 3410, 3150 (NH), 1700 (C=O), 1635 (C=N) cm^{-1}; NMR (TFA) δ 1.6–2.8 (m, 14 H), 8.65 (s, 1 H, NH), 8.8 (s, 1 H, NH), 9.8 (s, 1 H, NH).

Anal. Calcd for $C_{12}H_{17}N_3O$: C, 65.72; H, 7.82; N, 19.16. Found: C, 66.03; H, 7.93; N, 19.17.

The acid-insoluble material consisted of 0.65 g (32%) of unreacted starting material.

Acknowledgment. We are grateful to Professors A. Commeyras and W. Purdy, from whom we learned of the simplex method, to Dr. N. E. Lawson, for discussion and for a copy of the report of C. D. Hendrix,[14] to Professor S. Weber, who provided a computer program for application of the simplex method, to Julian Adams for preliminary experimentation, and to the Natural Sciences and Engineering Research Council of Canada for financial support.

Note Added in Proof. It has just come to our attention that simplex and other optimization procedures have been applied by Carlson et al.[23] to the synthesis of enamines from methyl ketones.

Registry No. 3, 700-58-3; **5** (RR = $C_{10}H_{14}$), 73367-52-9; **5** (RR = $(CH_2)_5$), 23000-17-1; A (RR = $C_{10}H_{14}$), 24779-92-8; C (RR = $C_{10}H_{14}$), 24779-93-9; C (RR = $C_{10}H_{14}$) *p*-toluenesulfonate, 73367-53-0; G (RR = $C_{10}H_{14}$), 73367-54-1; G (RR = $(CH_2)_5$), 73367-55-2.

Supplementary Material Available: Conditions and yields for 52 experiments involving cyclohexanone and 112 experiments involving adamantanone (13 pages). Ordering information is given on any current masthead page.

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Photoalkylation of *s*-Triazolo[4,3-*b*]pyridazine with Alcohols and Glycols[1a]

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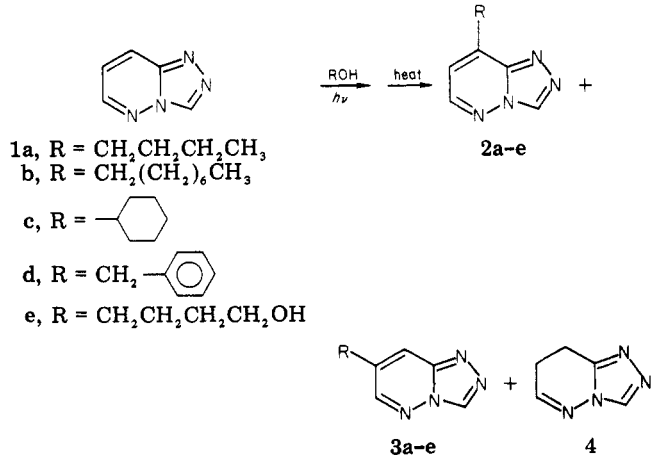
s-Triazolo[4,3-*b*]pyridazine (**1**) was irradiated in 1-butanol to yield 8- and 7-(1′-hydroxybutyl)-7,8-dihydro-*s*-triazolo[4,3-*b*]pyridazines (**5** and **6**) which were isolated and characterized. When this mixture was heated to 260 °C, 8- and 7-*n*-butyl-*s*-triazolo[4,3-*b*]pyridazines (**2a** and **3a**) were isolated. Similar 8- and 7-alkylated compounds were prepared from the photoalkylation of **1** with 1-octanol (**2b** and **3b**), cyclohexanol (**2c** and **3c**), benzyl alcohol (**2d** and **3d**), and 1,4-butanediol (**2e** and **3e**). 7,8-Dihydro-*s*-triazolo[4,3-*b*]pyridazine (**4**) was also isolated from the reaction mixture of the irradiation of **1** with cyclohexanol and with benzyl alcohol. 8-*n*-Butyl-7-methyl- and 7,8-di-*n*-butyl-*s*-triazolo[4,3-*b*]pyridazines (**7** and **8**) have also been prepared. When **2e** or a mixture of **2e** and **3e** was irradiated for 4 h and the reaction mixture heated, 7,8,9,10-tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (**9**) was the only product isolated. Compound **9** was also prepared by an independent synthesis.

The photoalkylation of N-heterocyclic aromatic compounds has been recently treated in reviews by Padwa[1b] and Carnelisse.[2] Photochemical substitutions in purines and purine nucleosides have been reviewed,[3] and the photoinduced methylation of pyrimidines and condensed pyrimidine compounds in acidified methanol has been studied in detail.[4] The photoalkylation of pyridazine in acidified methanol to yield 4-methyl-, 5-methyl-, and 4,5-dimethylpyridazines has been reported by Tsuchiya and co-workers.[5] In addition to using alcohols, other workers have shown that photoalkylation reactions also take place in carboxylic acids,[6] ethers,[7] hydrocarbons,[8] and amines.[9]

Scheme I. Photoalkylation Products



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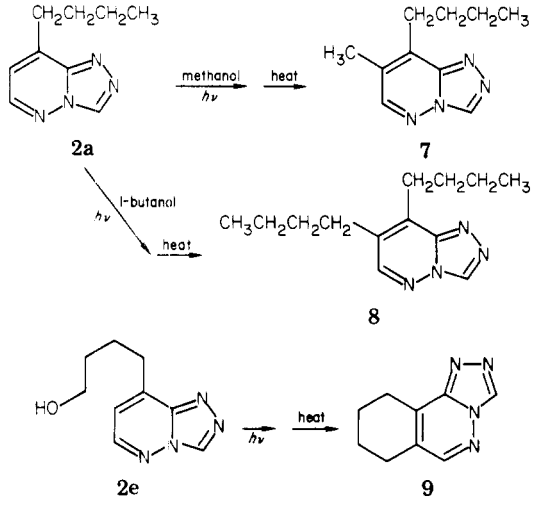
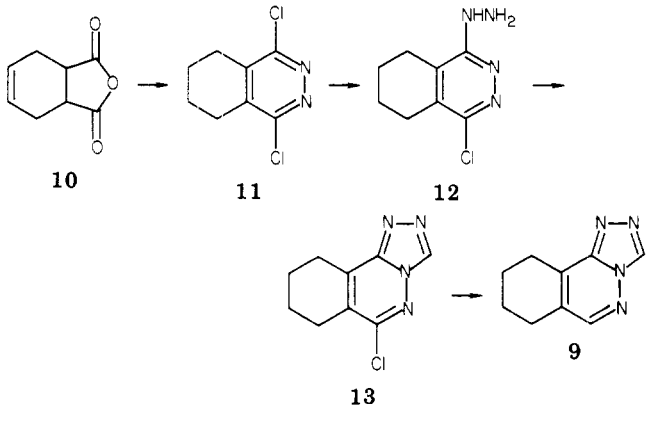
Scheme II. Additional Photochemical Reactions



Scheme III. Synthesis of 9



We have been interested in the photocycloaddition of alkenes to s-triazolo[4,3-b]pyridazine (1)[10] as well as the irradiation of 1 in methanol, ethanol, and 2-propanol, yielding the corresponding 8- and 7-alkylated photoproducts.[11] We now report the irradiation of compound 1 in 1-butanol, 1-octanol, cyclohexanol, benzyl alcohol, and 1,4-butanediol. After sublimination, the reaction mixture gave the corresponding 8- and 7-substituted s-triazolo[4,3-b]pyridazines (2 and 3 in Scheme I) and, in two instances, 7,8-dihydro-s-triazolo[4,3-b]pyridazine (4). The intermediate 8- and 7-(1-hydroxybutyl)-7,8-dihydro-s-triazolo[4,3-b]pyridazine compounds (5 and 6) initially formed when 1 was irradiated in 1-butanol were also isolated and characterized. 7,8-Disubstituted s-triazolo[4,3-b]pyridazines (7 and 8) were formed from the 8-n-butyl compound (2a; see Scheme II). 7,8,9,10-Tetrahydro-s-triazolo[3,4-a]phthalazine (9) was the only product from the irradiation of either compound 2a or a mixture of 2e and 3e. Compound 9 was prepared by an independent synthesis from cis-4-cyclohexene-1,2-dicarboxylic anhydride (see Scheme III).

Results and Discussion

The starting material (1) was dissolved in dichloromethane and irradiated in the appropriate alcohol until no starting material remained in the solution as monitored by gas–liquid chromatography (GLC). The solvent was then removed, and the gummy residue was sublimed and then separated by GLC or preparative thin-layer chromatography (TLC). The products were analyzed by ^1H and ^{13}C NMR and infrared (IR) and mass spectroscopy. The reactions are shown in Schemes I and II.

The proposed structures of the products were consistent with their spectra. The ^1H NMR spectra for alkylated derivatives of compound 1 are very distinctive.[11,12] The hydrogens on the alkyl chain are observed at δ 3.1 and 1.9 for the α and β protons of the 8-alkylated products (**2a** and **2b**) and at δ 2.7 and 1.6 for the 7-alkylated products (**3a** and **3b**). Resonance structures of 1 show that positions 6 and 8 are considerably electron deficient. Therefore, one would expect the α hydrogens on the alkyl substituent at position 8 to be further downfield that those substituted at position 7. However, in order to explain adequately the unusual downfield shift of the β hydrogens in these alkyl-substituted compounds another explanation is needed.

Feiring and Ciabattoni found that β hydrogens on the alkyl chain were not significantly affected by the position of attachement on the pyridazine ring.[13] Models show that the β hydrogens of **2a,b** can be in close proximity to N_1, while this is not possible for the β hydrogens of **3a,b**. We believe that the nitrogen in position 1 is deshielding the β protons on the alkyl side chain of the 8-alkylated products. McDonald and co-workers[14] demonstrated such a deshielding effect of the pyridine nitrogen in the 2- and 4-pentylpyridines.

The ^{13}C NMR spectra of the 8- and 7-n-butyl-s-triazolo[4,3-b]pyridazines (**2a** and **3a**) were obtained, and the chemical shifts were compared to those of the parent compound 1.[15] The α and β carbons of the alkyl chains of **2a** and **3a** were assigned by selective decoupling experiments. The ^{13}C NMR spectrum of **3a** shows two distinct peaks for the α and β carbons. However, in the 8-n-butyl isomer (**2a**) the β carbon is barely distinguishable from the α carbon. We believe that the same deshielding effect of N_1, which causes the β protons in the ^1H NMR spectrum of the 8-alkylated products to be shifted unusually far downfield, is also causing the β carbon to be shifted downfield.

The initial photochemical reaction of 1 with 1-butanol led to a mixture of 8- and 7-(1′-hydroxybutyl)-7,8-dihydro-s-triazolo[4,3-b]pyridazines (**5** and **6**). These types of compounds were postulated by us in our previous publication.[11] These compounds were separated by chromatography from the reaction mixture after irradiation but before the mixture was sublimed. When these hydroxybutyl intermediates (**5** and **6**) were heated and sublimed, compounds **2a** and **3a** were isolated and characterized. In the ^1H NMR spectra of **5** and **6**, the peaks at δ 8.4 and 7.7 are indicative of the hydrogens at positions 3 and 6, respectively. The hydrogens in the 7 and 8 positions appear as multiplets between δ 2.7 and 3.4, which is characteristic of the 7,8-dihydro compound **4**.[11] The hydroxy hydrogen appeared at δ 4.3 and was exchangeable

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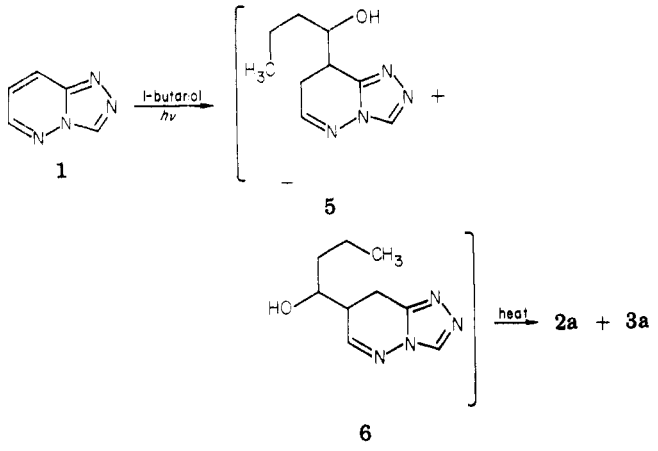

1 5 6

in deuterated water. The remaining hydrogens of the butyl group appeared at the expected chemical shifts.

The mass spectra of hydroxybutyl intermediates **5** and **6** gave characteristic fragmentation patterns for an alcohol in the electron impact mode and an $(M + 1)^+$ base peak in the chemical ionization mode. In addition to a small parent peak at m/e 194, the electron impact mass spectra of a mixture of **5** and **6** exhibited peaks at m/e 151 [$(M - C_3H_7)^+$], 121 [$(M - C_4H_9O)^+$] (the base peak), and 73 [$(M - C_5H_5N_4)^+$]. These peaks are consistent with the assigned structures for compounds **5** and **6**.

When **1** was irradiated with cyclohexanol and benzyl alcohol, 7,8-dihydro-*s*-triazolo[4,3-*b*]pyridazine (**4**) was also formed and characterized. With benzyl alcohol, **4** is believed to have been formed from an 8-(1′-hydroxybenzyl)-7,8-dihydro-*s*-triazolo[4,3-*b*]pyridazine intermediate (similar to **5**) by a reverse aldol-type condensation reaction.[11] We made no attempt to isolate the benzaldehyde or cyclohexanone byproducts since a similar reaction was observed for the reaction of **1** with 2-propanol, which gave acetone.[11]

The irradiation of **2e** or a mixture of **2e** and **3e** gave 7,8,9,10-tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (**9**) as the only product. This reaction involves ring closure to form a cyclic hydroxy intermediate which then loses the elements of water and rearomatizes upon heating to yield **9**, which has not previously been reported. The fully aromatic compound, *s*-triazolo[3,4-*a*]phthalazine, has been reported.[16,17]

We have independently prepared compound **9** from *cis*-4-cyclohexene-1,2-dicarboxylic anhydride (**10**; see Scheme III). Compound **10** was isomerized to 1-cyclohexene-1,2-dicarboxylic anhydride[18] which was then converted into 1,4-dichloro-5,6,7,8-tetrahydrophthalazine (**11**).[19] Compound **11** was treated with 95% hydrazine in refluxing toluene to produce 4-chloro-1-hydrazino-5,6,7,8-tetrahydrophthalazine (**12**) in high yield. The desired product **9** was formed by ring closure of **12** with triethyl orthoformate to yield **13**, followed by dehalogenation with hydrogen and 10% palladium on carbon.

We expected at least some 6-substituted products from the photoalkylation process; however, none were detected. These results closely parallel radical addition reactions to compound **1**. It has been shown that compound **1** reacts with radicals to give mainly 8-substituted products with some substitution in position 7 but very little in position 6.[12]

Photoinduced phenylation of **1** was not successful, with the irradiation of **1** in phenol giving no detectable reaction. However, Tisler and co-workers have recently reported the successful homolytic phenylation of **1**, with the reaction taking place preferentially at position 8 and with a lower selectivity for positions 7 and 3.[20] No reaction was observed in the irradiation of **1** with 1-butanethiol, butanal, or pentanoic acid.

8-*n*-Butyl-*s*-triazolo[4,3-*b*]pyridazine (**2a**) was also formed in the irradiation of **1** with *n*-butylamine and *n*-butyl ether. The product was isolated by GLC and exhibited ^{1}H NMR and mass spectra identical with the spectra obtained from an authentic sample of **2a**. The 7-*n*-butyl isomer (**3a**) was not detected.

Experimental Section

All IR spectra were obtained on a Beckman Acculab 2 spectrophotometer. The ^{1}H NMR spectra were obtained on a Varian EM-390 spectrometer and the ^{13}C NMR spectra on a JEOL 90Q Fourier transform spectrometer. All ^{1}H and ^{13}C NMR spectra were obtained in deuteriochloroform with tetramethylsilane as internal reference. A Varian Model 1700 gas chromatograph equipped with a thermal conductivity detector and a 6 ft × $^1/_4$ in. column packed with 10% OV-17 on 80/100-mesh high-performance Chromosorb W/AW (or 80/100-mesh Varaport 30/AW) was used for all the separations. The mass spectra were obtained on a CEC-20-110 C high-resolution mass spectrometer except for the hydroxybutyl intermediates which were obtained on a HP 5982 mass spectrometer in both the electron impact (EI) and chemical ionization (CI) modes. All UV spectra were recorded on a Beckman DU spectrophotometer, with absorptions less than 220 nm not being reported. All melting points are uncorrected. The elemental analyses were performed by MHW Laboratories.

All reactions were carried out with a Hanovia 450-W lamp in a water-cooled immersion reactor containing a Pyrex filter. In most cases, 200 mg of compound **1** and 10 g of the appropriate alcohol, which was freshly distilled, were dissolved in approximately 100 mL of reagent dichloromethane. The irradiation was continued until no starting compound **1** was observed when the reaction mixture was subjected to GLC, usually requiring about 10 h of irradiation. The reaction mixture was then sublimed at 260 °C (1 mm) to yield a mixture of the observed products.

In some cases, sufficient separation was obtained by using preparative TLC on silica gel F-254 plates with chloroform–methanol (9:1) as the solvent system. However, for total purification of the observed isomers, the reaction mixture was analyzed by GLC. The GLC analysis was carried out by using linear temperature programming of 6 °C/min from 180 °C to a final temperature of 265 °C. Each reaction with its isolated products is given below. Except where noted, the yields are relative percentages and were calculated from the GLC data as a function of individual peak area divided by the total peak area and are expressed as a percent.

1-Butanol Photoproducts. The reaction with 1-butanol gave three peaks which were isolated by GLC. Peak 1 (5% of the total peak area) proved to be starting compound **1**. Peak 2 (75%, compound **2a**) exhibited the following spectra: ^{1}H NMR δ 9.10 (s, 1 H, H_3), 8.27 (d, 1 H, H_6), 6.90 (d, 1 H, H_7), 3.13 (t, 2 H, $H_{1'}$), 1.88 (quintet, 2 H, $H_{2'}$), 1.46 (sextet, 2 H, $H_{3'}$), 0.98 (t, 3 H, $H_{4'}$); ^{13}C NMR δ 146.2 (C_6), 145.1 (C_{8a}), 141.3 (C_8), 138.9 (C_3), 117.9 (C_7), 30.3 ($C_{1'}$), 30.2 ($C_{2'}$), 22.5 ($C_{3'}$), 13.7 ($C_{4'}$).

Anal. Calcd for $C_9H_{12}N_4$: C, 61.34; H, 6.87. Found: C, 61.14; H, 7.07.

Peak 3 (20%, compound **3a**) exhibited the following spectra: ^{1}H NMR δ 9.09 (s, 1 H, H_3), 8.24 (s, 1 H, H_6), 7.85 (s, 1 H, H_8), 2.74 (t, 2 H, $H_{1'}$), 1.23–1.85 (m, 4 H, $H_{2',3'}$), 0.99 (t, 3 H, $H_{4'}$); ^{13}C NMR δ 148.0 (C_6), 144.3 (C_{8a}), 138.2 (C_3), 136.1 (C_7), 121.3 (C_8),

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32.7 ($C_{1'}$), 31.8 ($C_{2'}$), 22.2 ($C_{3'}$), 13.7 ($C_{4'}$); mol wt calcd for $C_9H_{12}N_4$, 176.1062; found, 176.1064.

1-Octanol Photoproducts. The reaction with 1-octanol (Fisher) gave one major peak and two minor peaks. Peak 1 (5%) proved to be starting compound **1**. Peak 2 (85%, compound **2b**) exhibited the following spectrum: ^{1}H NMR δ 9.19 (s, 1 H, H_3), 8.36 (d, 1 H, H_6), 6.97 (d, 1 H, H_7), 3.13 (t, 2 H, $H_{1'}$), 1.88 (quintet, 2 H, $H_{2'}$), 1.26 (m, 10 H, $H_{3'-7'}$), 0.86 (t, 3 H, $H_{8'}$).

Anal. Calcd for $C_{13}H_{20}N_4$: C, 67.20; H, 8.68. Found: C, 66.96; H, 8.82.

Peak 3 (10%, compound **3b**) exhibited the following spectra: ^{1}H NMR δ 9.15 (s, 1 H, H_3), 8.28 (s, 1 H, H_6), 7.88 (s, 1 H, H_8), 2.74 (t, 2 H, $H_{1'}$), 1.63 (m, 2 H, $H_{2'}$), 1.28 (m, 10 H, $H_{3'-7'}$), 0.86 (t, 3 H, $H_{8'}$); mol wt calcd for $C_{13}H_{20}N_4$, 232.168 78; found, 232.167 66.

Cyclohexanol Photoproducts. Four peaks were isolated by GLC from the reaction with cyclohexanol. Peak 1 (10%) proved to be starting compound **1**. Peak 2 (18%, compound **4**) exhibited the same ^{1}H NMR spectra as an authentic sample of 7,8-dihydro-s-triazolo[4,3-b]pyridazine.[11] Peak 3 (65%, compound **2c**) exhibited the following spectrum: ^{1}H NMR δ 9.13 (s, 1 H, H_3), 8.35 (d, 1 H, H_6), 6.92 (d, 1 H, H_7), 3.35 (m, 1 H, $H_{1'}$), 1.16–2.30 (m, 10 H, $H_{2'-6'}$).

Anal. Calcd for $C_{11}H_{14}N_4$: C, 65.32; H, 6.98. Found: C, 65.17; H, 6.85.

Peak 4 (7%, compound **3c**) exhibited the following spectra: ^{1}H NMR δ 9.06 (s, 1 H, H_3), 8.29 (s, 1 H, H_6), 7.86 (s, 1 H, H_8), 2.71 (m, 1 H, $H_{1'}$), 1.06–2.19 (m, 10 H, $H_{2'-6'}$); mol wt calcd for $C_{11}H_{14}N_4$, 202.121 84; found, 202.122 40.

Benzyl Alcohol Photoproducts. The reaction with benzyl alcohol (Mallinckrodt) gave four peaks which were isolated by GLC. Peak 1 (7%) proved to be starting compound **1**. Peak 2 (40%) was identified by ^{1}H NMR to be compound **4**.[11] Peak 3 (33%, compound **2d**) exhibited the following spectra: ^{1}H NMR δ 9.15 (s, 1 H, H_3), 8.28 (d, 1 H, H_6), 7.37 (m, 5 H, Ar H), 6.74 (d, 1 H, H_7), 4.46 (s, 2 H, $H_{1'}$); mol wt calcd for $C_{12}H_{10}N_4$, 210.090 54; found, 210.089 08.

Peak 4 (20%, compound **3d**) exhibited the following spectra: ^{1}H NMR δ 9.03 (s, 1 H, H_3), 8.23 (s, 1 H, H_6), 7.79 (s, 1 H, H_8), 7.28 (m, 5 H, Ar H), 4.03 (s, 2 H, $H_{1'}$); mol wt calcd for $C_{12}H_{10}N_4$, 210.090 54; found, 210.089 92.

1,4-Butanediol Photoproducts. The reaction with 1,4-butanediol (Matheson Coleman and Bell) was not chromatographable by GLC; consequently the products were separated by preparative TLC. Compound **2e** (32 mg, 10% overall yield) was isolated in high purity by this method and exhibited the following spectra: IR 3300 cm^{-1} (OH); ^{1}H NMR δ 9.13 (s, 1 H, H_3), 8.34 (d, 1 H, H_6), 6.99 (d, 1 H, H_7), 4.10 (br s, 1 H, OH), 3.75 (t, 2 H, $H_{4'}$), 3.16 (t, 2 H, $H_{1'}$), 1.60–2.16 (m, 4 H, $H_{2',3'}$); mass spectrum (EI), m/e 192 $(M)^+$, 161 $[(M - CH_2OH\cdot)^+]$; mol wt calcd for $C_9H_{12}N_4O$, 192.1011; found, 192.1007.

A mixture of compounds **2e** and **3e** (18 mg, ratio 45:55) was also isolated from the preparative TLC separation. The ^{1}H NMR spectrum of the mixture showed the peaks assigned to compound **2e** as well as the following peaks which can be assigned to compound **3e**: δ 9.11 (s, 1 H, H_3), 8.32 (s, 1 H, H_6), 7.95 (s, 1 H, H_8), 4.07 (s, 1 H, OH), 3.72 (t, 2 H, $H_{4'}$), 2.82 (t, 2 H, $H_{1'}$), 1.58–2.09 (m, 4 H, $H_{2',3'}$). Compound **3e** could not be further purified.

Irradiation of 2a in Methanol. 8-n-Butyl-s-triazolo[4,3-b]pyridazine (**2a**, 65 mg) was irradiated in 50 mL of methanol for 6 h. After the reaction mixture was sublimed at 260 °C (1 mm) for 2 h, it was subjected to GLC analysis. Two peaks were observed and characterized. Peak 1 (20%) proved to be starting compound **2a**. Peak 2 (80%, compound **7**) exhibited the following spectra: ^{1}H NMR δ 9.04 (s, 1 H, H_3), 8.19 (s, 1 H, H_6), 3.13 (t, 2 H, $H_{1'}$), 2.39 (s, 3 H, CH_3), 1.34–1.83 (m, 4 H, $H_{2',3'}$), 0.97 (t, 3 H, $H_{4'}$); mol wt calcd for $C_{10}H_{14}N_4$, 190.121 84; found, 190.123 33.

Irradiation of 2a in 1-Butanol. 8-n-Butyl-s-triazolo[4,3-b]pyridazine (**2a**, 40 mg) was irradiated in 10 g of 1-butanol for 10 h. GLC analysis of the sublimed photoproduct gave two peaks. Peak 1 (15%) proved to be starting compound **2a**. Peak 2 (85%, compound **8**) exhibited the following spectra: ^{1}H NMR δ 9.08 (s, 1 H, H_3), 8.17 (s, 1 H, H_6), 3.08 (t, 2 H, $H_{1'(8)}$), 2.73 (t, 2 H, $H_{1'(7)}$), 1.16–1.90 (m, 8 H, $H_{2',3'}$), 0.97 (t, 6 H, $H_{4'}$); mol wt calcd for $C_{13}H_{20}N_4$, 232.168 79; found, 232.168 29.

7,8-Di-n-butyl-s-triazolo[4,3-b]pyridazine (**8**) was also prepared from the irradiation of a 100-mg mixture of compounds **2a** and **3a** under the same conditions as described above.

Irradiation of 2e. 8-(4'-Hydroxybutyl)-s-triazolo[4,3-b]-pyridazine (**2e**, 40 mg) was irradiated in dichloromethane for 4 h. The reaction mixture was then sublimed and separated by GLC, with two peaks being characterized. Peak 1 (15%) proved to be starting compound **2e**. Peak 2 (85%, compound **9**) exhibited the following spectra: ^{1}H NMR δ 9.00 (s, 1 H, H_3), 8.06 (s, 1 H, H_6), 3.12 (t, 2 H, H_{10}), 2.75 (t, 2 H, H_7), 1.94 (quintet, 4 H, $H_{8,9}$); mol wt calcd for $C_9H_{10}N_4$, 174.090 54; found, 174.089 60.

7,8,9,10-Tetrahydro-s-triazolo[3,4-a]phthalazine (**9**) was also isolated from the irradiation (4 h) of 135 mg of a mixture of compounds **2e** and **3e**. The reaction mixture was sublimed and then separated by preparative TLC. The crude product (10 mg, 8%) isolated from the TLC was purified by GLC to give the same ^{1}H NMR spectrum as given above.

Isolation of Hydroxybutyl Intermediates 5 and 6. Compound **1** (0.40 g) was irradiated in 10 g of 1-butanol for 10 h. The solvent and excess alcohol were removed under vacuum, yielding 0.65 g of a brown gum. This material was then analyzed on a 3 ft × $^1/_2$ in. column packed with silica gel ($CHCl_3$) and eluted with a mixture of chloroform and methanol (9:1). A mixture (0.26 g, 40% overall yield) of 8-(1'-hydroxybutyl)- and 7-(1'-hydroxybutyl)-7,8-dihydro-s-triazolo[4,3-b]pyridazines (**5** and **6**) was isolated. This mixture, which could not be further separated, exhibited the following spectra: IR 3300 cm^{-1} (OH); ^{1}H NMR δ 8.35 (d, 1 H, H_3), 7.60 (t, 1 H, H_6), 4.26 (br s, 1 H, OH, exchanged in D_2O), 4.01 (m, 1 H, $H_{1'}$), 3.25 (m, 1 H, H_8), 2.79 (m, 2 H, H_7), 1.54 (m, 4 H, $H_{2',3'}$), 0.96 (t, 3 H, $H_{4'}$); mass spectrum (EI), m/e (relative intensity) 194 (M^+, 2.2), 177 (4.5), 151 (8.1), 122 (80.5), 121 (100), 95 (15.6), 73 (11.2), 55 (35.6), 45 (19.5); mass spectrum (CI), m/e (relative intensity) 235 (M + 41, 3.3), 223 (M + 29, 14.2), 209 (1.5), 195 (M + 1, 100), 177 (2.5), 151 (2.4), 123 (7.9), 122 (2.2), 121 (1.6).

Anal. Calcd for $C_9H_{14}N_4O$: C, 55.65; H, 7.26. Found: C, 55.44; H, 7.22.

Preparation of 6-Chloro-7,8,9,10-tetrahydro-s-triazolo-[3,4-a]phthalazine (13). 1-Cyclohexene-1,2-dicarboxylic anhydride[18] was converted to 4-hydroxy-5,6,7,8-tetrahydro-1-(2*H*)-phthalazinone by refluxing it in water with hydrazine sulfate.[19] We found that using hydrazine sulfate was preferred over the procedure by Horning[21] in which hydrazine hydrate was used in forming the phthalazine ring system. 4-Hydroxy-5,6,7,8-tetrahydro-1(2*H*)-phthalazinone was treated with phosphorus oxychloride to yield **11**.[19]

1,4-Dichloro-5,6,7,8-tetrahydrophthalazine (**11**, 10.0 g) was treated with 4.10 g of 95% hydrazine in refluxing toluene for 16 h. The reaction mixture was then cooled to room temperature and filtered to yield 7.8 g (80%)[22] of an orange solid which proved to be 4-chloro-1-hydrazino-5,6,7,8-tetrahydrophthalazine (**12**). The crude product (mp 106–108 °C), which was not purified further, exhibited the following spectra: ^{1}H NMR δ 3.85 (br s, 3 H, $NHNH_2$), 2.63 (m, 2 H, H_8), 2.36 (m, 2 H, H_5), 1.81 (m, 4 H, $H_{6,7}$); mass spectrum (EI), m/e (relative intensity) 200 (33.0), 199 (15.7), 198 (M^+, 100.0), 197 (15.2), 182 (23.1), 118 (39.1), 91 (41.9).

4-Chloro-1-hydrazino-5,6,7,8-tetrahydrophthalazine (**12**, 5.0 g) was refluxed for 6 h in 100 mL of triethyl orthoformate. The solvent was removed under vacuum and the resulting solid recrystallized from 100% ethanol to yield 3.8 g (72%) of **13** as a light brown solid (mp 116–118 °C). An analytical sample (mp 122–123 °C) was prepared by preparative TLC and exhibited the following spectra: IR 3130, 2940, 2860, 1595, 1525, 1455, 1410, 1265, 1210, 1180, 990, 945, 800 cm^{-1}; ^{1}H NMR δ 8.89 (s, 1 H, H_3), 3.14 (m, 2 H, H_{10}), 2.74 (m, 2 H, H_7), 1.92 (m, 4 H, $H_{8,9}$); UV (EtOH) λ_{max}(pH 1) 270 nm (ϵ 4350), λ_{max}(pH 7) 292 (3800), λ_{max}(pH 11) 292 (3800); mass spectrum (EI), m/e (relative intensity) 210 (33.2), 209 (21.9), 208 (M^+, 100.0), 207 (35.5), 193 (7.6), 180 (23.4), 173 (11.9).

(21) R. H. Horning and E. D. Amstutz, *J. Org. Chem.*, **20**, 707 (1955).

(22) The yields were lower when ethanol was used as the solvent, with considerable amounts of unreacted started material, **11**, being recovered. If the reaction mixture, with toluene or ethanol as the solvent, was cooled to 0 °C, unreacted starting material, **11**, also precipitated out of the solvent with the product. Minor amounts of 1,4-dihydrazino-5,6,7,8-tetrahydrophthalazine (mp, shrinks at 95 °C, decomposes at 260 °C) were detected and analyzed by mass spectra (EI) and ^{1}H NMR.

Anal. Calcd for $C_9H_9N_4Cl$: C, 51.80; H, 4.35. Found: C, 51.60; H, 4.24.

Preparation of 7,8,9,10-Tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (9). 6-Chloro-7,8,9,10-tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (**13**, 1.0 g) and 100 mg of 10% palladium on carbon were added to 150 mL of 95% ethanol, and the pH of the solution was adjusted to 9 with ammonium hydroxide. The hydrogenation was carried out in a Paar apparatus with an initial pressure of 45 psi of H_2 and continued for 2 h. The reaction mixture was filtered through Celite and the solvent removed under vacuum. The residue was dissolved in water and extracted with chloroform to yield 0.69 g (83%) of a light brown solid (mp 105–108 °C). The product was then sublimed at 100 °C (1 mm) to yield a white solid (mp 132–134 °C) which exhibited the following spectra: IR 3120, 2940, 2870, 1615, 1540, 1495, 1450, 1420, 1340, 1185, 1170, 980, 935 cm^{-1}; ^1H NMR δ 9.01 (s, 1 H, H_3), 8.08 (s, 1 H, H_6), 3.12 (m, 2 H, H_{10}), 2.76 (m, 2 H, H_7), 1.94 (m, 4 H, $H_{8,9}$); ^{13}C NMR δ 148.1 (C_6), 144.8 (C_{10b}), 138.5 (C_3), 133.6 and 129.3 (C_{6a} and C_{10a}), 25.7, 23.1, 21.6, and 20.7 (C_{7-10}); UV (EtOH) λ_{max}(pH 1) 264 nm (ϵ 5100), λ_{max}(pH 7) 237 (3600), 282 (3100), λ_{max}(pH 11) 282 (3250); mass spectrum (EI), *m/e* (relative intensity) 175 (12.1), 174 (M^+, 100.0), 173 (43.5), 146 (36.9).

Anal. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.79; N, 32.16. Found: C, 61.89; H, 5.65; N, 32.36.

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Registry No. **1**, 274-83-9; **2a**, 73453-17-5; **2b**, 73453-18-6; **2c**, 73453-19-7; **2d**, 73453-20-0; **2e**, 73453-21-1; **3a**, 73453-22-2; **3b**, 73453-23-3; **3c**, 73453-24-4; **3d**, 73453-25-5; **3e**, 73453-26-6; **4**, 50357-95-4; **5**, 73453-27-7; **6**, 73453-28-8; **7**, 73453-29-9; **8**, 73453-30-2; **9**, 73075-03-3; **10**, 935-79-5; **11**, 67279-24-7; **12**, 66597-78-2; **13**, 66978-72-1; 1-butanol, 71-36-3; 1-octanol, 111-87-5; cyclohexanol, 108-93-0; benzyl alcohol, 100-51-6; 1,4-butanediol, 110-63-4; 4-hydroxy-5,6,7,8-tetrahydro-1(2*H*)-phthalazinone, 73453-31-3; hydrazine, 302-01-2; methanol, 67-56-1.

Photochemistry of 11α- and 11β-Hydroxy Steroidal 1,4-Dien-3-ones and 11α- and 11β-Hydroxy Steroidal Bicyclo[3.1.0]hex-3-en-2-ones in Neutral and Acidic Media[1a]

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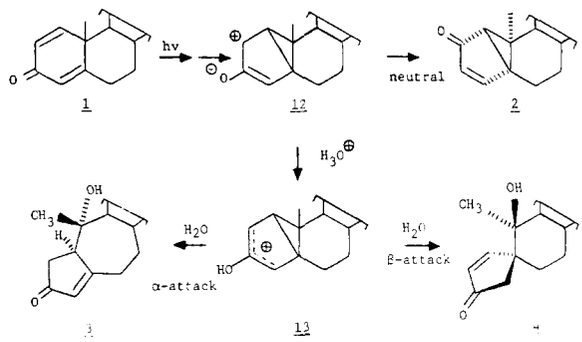
The photolysis of prednisolone, **1b**, its 21-acetate, **1c**, and 11α-hydroxypregna-1,4-dien-3,20-dione, **1d**, in dioxane yielded the lumiproducts **2b**, **2c**, and **2d**, respectively. Further photoisomerization of the 11β-hydroxy lumiproducts **2b** and **2c** in dioxane gave 17α,21-dihydroxy-1β,11β-oxy-10α-pregna-2,20-dione, **9a**, and 21-acetoxy-17α-hydroxy-1β,11β-oxy-10α-pregna-2,20-dione, **9b**, respectively, whereas the 11α-hydroxy lumiproduct **2d** yielded 2,11α-dihydroxy-4-methyl-19-norpregna-1,3,5(10)-trien-20-one, **7a**. Photolysis of **1b** and **1c** in acidic conditions afforded the 1β,11β-oxy steroids **9a** and **9b** as the major photoproducts together with the expected rearranged bicyclo[5.3.0] systems **3b** and **3c** and spiro steroids **4b** and **4c**, respectively. Photolysis of **1d** under acidic conditions only afforded **3d** and **4d**. The mechanism of these photoisomerization reactions is discussed. The influence of the 11α- and 11β-hydroxyl function on the photochemistry of the cross-conjugated cyclohexadienones and the bicyclo[3.1.0]hex-3-en-2-one systems in aqueous acetic acid and in dioxane, respectively, is explained.

The photochemistry of cross-conjugated cyclohexadienones has been intensely studied because of their facile and fascinatingly complex photochemical rearrangement reactions. These rearrangement reactions have been the topic of a number of excellent reviews.[2] Recently, the photochemistry of the medicinally important steroid prednisone acetate (**1a**) was reinvestigated by Williams et al.[1] The structure of lumiprednisone acetate[3] was revised to that of a bicyclo[3.1.0]hex-3-en-2-one ring A system (**2a**)

Scheme I. General Photoisomerization Paths of Cross-Conjugated Dienones



and a new photochemical rearrangement of this intermediate reported.[1] Since the photochemical reactions of cross-conjugated cyclohexadienones and their resulting lumiproducts are extremely sensitive to changes in struc-

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