trum showed this fraction to consist of 70.5% of α-cyanocinnamamide and 29.5% of ethyl α-cyanocinnamate. The after run (730 mg) is a pale yellow oil which crystallized gradually too. The nmr spectrum indicated this fraction to be composed of 27.7% of α-cyanocinnamamide and 72.3% of ethyl α-cyanocinnamate. Thus, α-cyanocinnamamide and ethyl α-cyanocinnamate were obtained in 56.7 and 43.3% yield in total.

3,5-Dicyano-5-ethoxycarbonyl-3-*p*-nitrobenzyl-4,6-diphenyl-2-oxopiperidine (8) and 3,5-Dicyano-5-ethoxycarbonyl-1,3-di-*p*-nitrobenzyl-4,6-diphenyl-2-oxopiperidine (9).[12] A mixture of 3.6 g (9.6 mmol) of **4a** and 21 g of anhydrous sodium carbonate in 100 ml of 95% ethanol was refluxed to produce a clear yellow solution. To this solution was added a hot solution of 42 g (20 mmol) of *p*-nitrobenzyl bromide in 100 ml of 95% ethanol. The mixture was refluxed for 3 hr on a steam bath. Pale yellow crystals precipitated out. The organic layer containing the yellow crystals was separated by decantation from the insoluble sodium carbonate while hot. Pale yellow crystals were collected by vacuum filtration from the ethanol solution, washed with a small amount of water, and then dried. The crude white crystals, mp 275–279°, weighed 1.01 g (yield 16.3%); 1.0 g of the crude crystals were recrystallized from 60 ml of acetone to afford 255 mg of a pure substance (**9**), mp 284–285°. The filtrate from the crude crystals stood at room temperature and precipitated white crystals, 1.24 g (yield 25.4%), mp 247–249°. The crude white crystals, 1.2 g, were recrystallized from 200 ml of 99% ethanol to give 930 mg of a pure substance (**8**), mp 265–267°, as white crystals. **9**, ir (Nujol) 2250 cm^{-1} (CN), 1745 cm^{-1} (ester C=O), 1655 cm^{-1} (amide C=O), 1605 cm^{-1} (C=C), 1520 and 1350 cm^{-1} (NO_2), 1260 or 1220 and 1110 cm^{-1} (ester C–O–C), 855 and 840 cm^{-1} (para-substituted benzene), 700 cm^{-1} (monosubstituted benzene). **8**, ir (Nujol) 2250 cm^{-1} (CN), 1733 cm^{-1} (ester C=O), 1695 cm^{-1} (amide C=O), 1520 and 1340 cm^{-1} (NO_2), 1250 and 1110 cm^{-1} (ester C–O–C), 850 cm^{-1} (para-substituted benzene), 700 cm^{-1} (monosubstituted benzene).

3-*p*-Nitrobenzyl-4-phenyl-2,6-dioxopiperidine (10). Compound **8**, 7.10 g (0.014 mol), was refluxed in a mixed solution of 50 ml of concentrated hydrochloric acid and 100 ml of acetic acid for 8 hr, to give a yellow solution which contained a small amount of insoluble substance **9**. After cooling, the insoluble **9** was filtered off, 500 ml of water was added to the filtrate, and the mixture was extracted with three or four portions of 200 ml of ether. The ethereal solution was dried and distilled, to give 4.60 g of the residue. The residue was dissolved into 10 ml of hot 95% ethanol, and stood for several days at room temperature to precipitate considerable amounts of crystals. The crystals were collected, washed with 5 ml of cold ethanol, and then dried. The crude product, mp 155–160°, 1.86 g (yield 41.1%), was recrystallized from acetone to give pure **10**: mp 191–192°; ir (Nujol) 3200 and 3100 cm^{-1} (NH), 1725 and 1685 cm^{-1} (imide C=O), 1959 cm^{-1} (C=C), 1510 and 1350 cm^{-1} (NO_2), 1320 cm^{-1} ($-CH_2-$), 1240 cm^{-1} (C—C–C—C), 1170 cm^{-1} (C—CH_2—C), 860 cm^{-1} (para-substituted benzene); uv max (95% C_2H_5OH), in neutral medium, 206 mμ (log ε 4.51), 275 (4.00); in alkaline medium, 206 mμ (4.67), 235 (4.14), 278 (4.05); in acidic medium, 205 m μ (4.43) and 276 (4.02); nmr (acetone-d_6) δ 9.61 (s, 2, NH), 8.01 and 7.25 (A_2B_2, 4, para-substituted benzene), 7.33 (s, 5, monosubstituted benzene), 3.45–3.73 (m, 6, CH_2—CH=CH—CH_2).

Registry No.—**1c**, 2286-35-3; **1d**, 2286-33-1; **2a**, 6731-58-4; **2b**, 21739-28-6; **2c**, 52906-62-4; **2d**, 52906-63-5; **3a**, 52906-64-6; **3b**, 6327-92-0; **3c**, 52906-65-7; **3d**, 52906-66-8; **4a**, 52906-67-9; **4b**, 52906-68-0; **4d**, 52906-69-1; **8**, 52906-70-4; **9**, 52906-71-5; **10**, 52906-72-6; benzaldehyde, 100-52-7; *p*-methoxybenzaldehyde, 123-11-5; *p*-chlorobenzaldehyde, 104-88-1; *p*-nitrobenzaldehyde, 555-16-8; ethyl cyanoacetate, 105-56-6; β-phenylglutaric acid, 4165-96-2; benzaldehyde 2,4-DNPH, 1157-84-2.

References and Notes

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(9) Microanalyses were performed by the Microanalytical Laboratories of Kyoto University; infrared spectra were determined by means of a Perkin Elmer 180 spectrometer, ultraviolet spectra by means of a Perkin Elmer 202 spectrometer, nmr spectra by means of a Hitachi R-20-B (60 MHz) and a JEOL PS-100 (100 MHz) spectrometer, and mass spectra by means of a Hitachi MU-6 spectrometer.
(10) "The Merck Index of Chemicals and Drugs," Merck, Rahway, N. J., 1952, p 296.
(11) E. H. Rodd, *Chem. Carbon Compounds, B*, **3**, 946 (1956).
(12) In a run using 7.5 g of **4a**, 8.6 g of *p*-nitrobenzyl bromide, and 4.2 g of anhydrous sodium carbonate in 150 ml of 95% ethanol, 9.77 g of product was obtained. Recrystallization from ethanol, under monitoring with ir spectra, afforded **8**, mp 264–265°, 6.514 g (yield 64.1%); and **9**, mp 275–278°, 0.857 g (yield 6.6%).

Studies Directed toward a Mitomycin Synthesis

Gerald J. Siuta, Richard W. Franck,* and Robert J. Kempton

Department of Chemistry, Fordham University, Bronx, New York 10458

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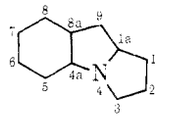
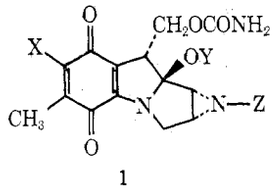
Alkylations of heterocyclic anion **7** with chloromethyl ethers followed by photooxidation afforded products with the essential framework of the mitomycin antibiotics. A generalized scheme for attaching aziridines to this carbon framework was developed. It involved a photochemical ring contraction of triazolines in the presence of a triplet quencher so as to suppress subsequent photochemistry of the tetracyclic products which may serve as mitomycin models.

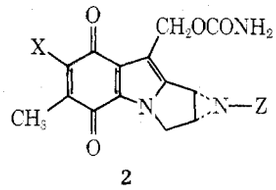
The mitomycins (**1**) are a class of antibiotics of wide-ranging activity. Since their structures were first elucidated in 1962,[1,2] there have been a variety of synthetic approaches to their framework and that of the closely related aziridinomitosenes (**2**). The majority of published routes are concerned with the formation of the tricyclic pyrrolo[1,2-*a*]indole ring system A. The choice of the ultimate bond to be



A



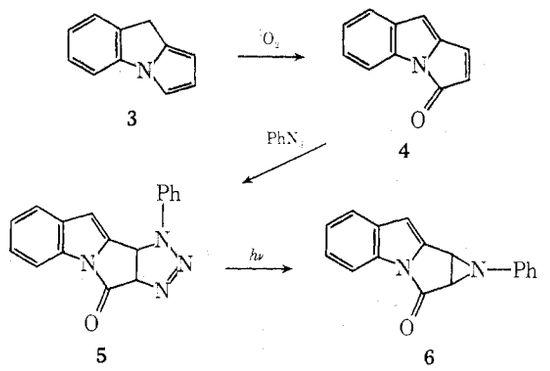
1



2

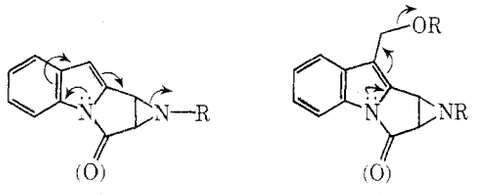
mitomycin A, X = CH_3O; Y = CH_3; Z = H
mitomycin B, X = CH_3O; Y = H; Z = CH_3
mitomycin C, X = NH_2; Y = CH_3; Z = H
porfiromycin, X = NH_2; Y = CH_3; Z = CH_3

Scheme I

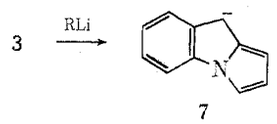


formed includes 8a–9,[3] 1a–9,[4] 4a–4,[5] 8a–9 and 4a–4,[6] 1a–4 and 3–4,[7] 1a–1 and 3–4,[8] 1–2 and 3–4,[4c,9] 4a–5 and 8a–8.[10] There has been a more limited program for introducing the carbamate at C-9[11,9a] and for achieving the correct quinone substitution pattern.[7,9a] There exist only two reports of aziridine introduction into a proper framework,[12] one of which comes from our laboratories and is summarized in Scheme I.[13]

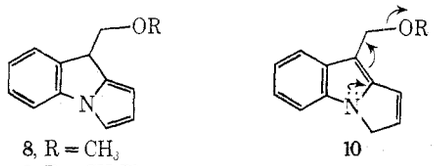
For the most part, these published efforts do not describe reactions that would be compatible with a complete synthesis of a mitomycin. In this paper we wish to describe our approaches to two structural features, solutions which we feel are transferable to a total synthesis. When our compound **6** is compared to a target aziridinomitosene **2**, the functions requiring further elucidation can be readily discerned. First, a one-carbon function, convertible to a carbamate, must be in place at C-9. Second, a substituent other than phenyl on the aziridine nitrogen must be obtained. The third and fourth problems, not dealt with in this article, are the development of a fully functionalized quinone (or potential quinone) that is compatible with the steps to be described in the sequel, and the removal of the carbonyl at C-3 which serves as a shield against internal eliminations initiated by indole nitrogen (B and C). The first problem



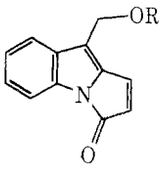
posed seemed capable of solution by using the carbanion **7**, formed upon treatment of heterocycle **3** with strong base.[9c,13,14] Previous work had shown that alkylation with



diethylaminoethyl chloride occurred at C-9 in high yield to afford a stable product. In our current work, alkylations were carried out on the lithium derivative with chloromethyl methyl ether and chloromethyl benzyl ether. In both cases, the presumed initial products **8** and **9** could not be



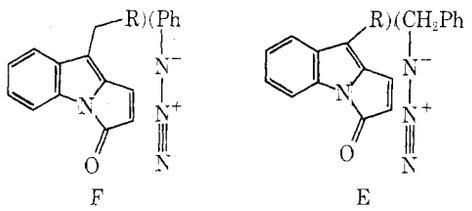
isolated since the crude reaction mixtures decomposed as the solvents were removed. It is difficult to rationalize any inherent instability for structures **8** or **9**. However, if a prototropic shift occurred, **8** and **9** could equilibrate with **10** which would be unstable because the ether would now be indolylic. Such a facile double-bond isomerization between the 3*H*- and 9*H*-pyrrolo[1,2-*a*]indole series has been inferred from work where a regiospecific synthesis of the parent heterocycle related to **10** (the 3H series) resulted in the clean isolation of **3** (the 9H series).[15] Since **8** and **9** could not be isolated, but their existence in dilute solution was presumed, the crude alkylation mixtures were photooxygenated. Work-up of the oxidation medium afforded the heterocycles **11** and **12** along with some **4** (derived from unalkylated **3**). Yields of **11** ranged from 8 to 24% while



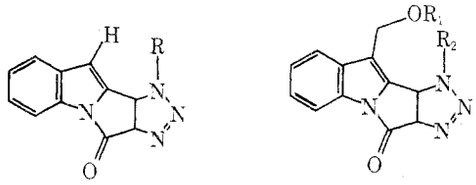
11, R = CH_3
12, R = CH_2Ph

those for **12** were 42–50%. The structural assignments were based on their nmr, ir, and uv spectra which were in good agreement with the data for **4**, save the missing indolic H at C-9 in the nmr, and the slight bathochromic shift in the uv (λ_{max} 360 for **11**, 355 for **4**).

With a direct introduction of the one-carbon function at C-9, the next step, dipolar addition of azides to the C-2,3 double bond, was investigated. In the parent series, phenyl and benzyl azide both added readily to **4**. In the current study, a steric hindrance to dipolar addition to **11** and **12** was observed. That is, phenyl azide was added with difficulty and in low yield whereas benzyl and methoxymethyl azide additions were smooth good yield processes. This can be rationalized as follows. The addition of the azides to the polarized double bond is regiospecific, thus the substituent on the azide and that at C-9 come in close proximity. The bulk of the benzyl group can bend away from the C-9 substituent (as in E) whereas the phenyl cannot (as in F). Of



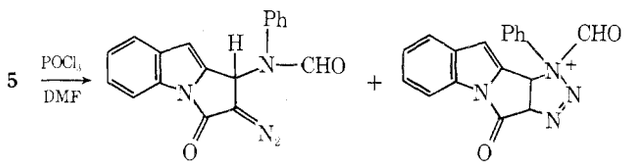
course, in the parent series, the group at C-9 is a proton, which offers no interference to either phenyl or benzyl. This sort of steric effect in dipolar additions does not seem to have been observed previous to this work (although it is not surprising).[16] A variety of triazolines **13** and **14** were



13a, R = CH_2Ph
b, R = CH_3

14a, $R_1 = CH_3$; $R_2 = Ph$
b, $R_1 = CH_3$; $R_2 = CH_2Ph$
c, $R_1 = CH_3$; $R_2 = CH_3$
d, $R_1 = CH_3$; $R_2 = CH_2OCH_2Ph$
e, $R_1 = CH_3$; $R_2 = CH_2OCH_3$
f, $R_1 = CH_2Ph$; $R_2 = CH_2Ph$

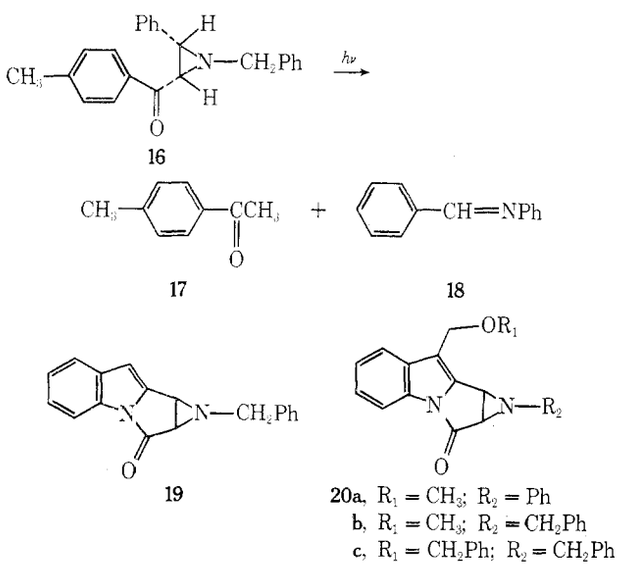
prepared using the general procedure of mixing azide and heterocycles **4**, **11**, or **12** in a minimum of solvent and either heating or allowing to stand at room temperature (depending on the thermal sensitivity of the azide). As an alternate to our alkylation procedure for introducing a carbon at C-9 at an early stage of the synthesis, there was attempted a functionalization of the "indolic" positions of **4** and **5** by a Vilsmeier formylation.[9a,11] In this event, **4** proved inert, but but **5** afforded a new product in 84% yield which had incorporated the required elements of CO. However, its nmr revealed *inter alia* the appearance of a formyl H at δ 8.93, more consistent with a formamide than an aldehyde, and the disappearance of the AB quartet characteristic of the protons of the triazoline ring fusion. Further an ir band at 4.78 μ, characteristic of diazo compounds, was present. We formulate the product as the *N*-formyl-*N*-phenylaminodiazo derivative **15**.



15 G

The formation of **15** can be rationalized by a ring opening of the formylated triazoline G. This behavior has been observed in the chemistry of triazolines; however, N_2 evolution usually takes place when there is no stabilizing group for the diazo function.[17]

To carry the main synthetic pathway forward, the photochemical ring contractions of the triazolines **13** and **14** were required. Our earlier work had shown that direct irradiation of **13a** was not successful in achieving an aziridine synthesis. This is consistent with work of Padwa[18] where irradiation of aziridines such as **16**, upon irradiation, resulted in the formation of products **17** and **18**. Thus we hypothesized that this type of reaction, shown by Padwa to proceed through a triplet excited state, must be quenched in order to maintain the integrity of our desired aziridines. In the event of irradiating triazolines **13a** and **14b,f** in 0.66 *M* solutions of piperylene in ethanol, there were obtained aziridines **19** and **20b,c**. Since **14a** was phenyl substituted, its conversion to **20a** did not require triplet quencher. The nmr spectral properties (Table I) were consistent with their formulation as aziridines, that is, upfield shifts and diminished coupling constants, criteria deduced in our previous paper.[9c,12] At this stage of our synthetic program, when it seemed that our two goals, enunciated at the start of this paper, had been achieved, it was decided to confront the third and fourth problems remaining for a total synthesis. Future reports will deal with this aspect of our work.



16

17 **18**

19

20a, $R_1 = CH_3$; $R_2 = Ph$
b, $R_1 = CH_3$; $R_2 = CH_2Ph$
c, $R_1 = CH_2Ph$; $R_2 = CH_2Ph$

Table I

Aziridine	δ, ppm	J_{AB}, Hz
6	3.80, 4.02	3.7
19	3.17, 3.38	4.3
20a	3.85, 4.20	3.4
20b	3.18, 3.48	4.5
20c	3.10, 3.39	4.5

Experimental Section

Commercially available starting materials were used as supplied, except where noted. Liquids were distilled through a vacuum-jacketed 4-in. Vigreux column; melting points were determined on a Fisher-Johns block, and, like boiling points, are corrected. Thin-layer chromatograms (tlc) in at least two different solvents or solvent pairs were performed on microscope slides coated with silica gel or alumina and were visualized with iodine vapor. Merck acid-washed alumina and Fisher 100–200 mesh silica gel were used for elution chromatography. Woelm fluorescent alumina and silica gel (activity II–III) were used for dry-column chromatography. Solutions were dried by washing with saturated sodium chloride solution (brine) followed by treatment with anhydrous sodium sulfate. Solvents were removed by rotary evaporation. Where noted, an atmosphere of dry nitrogen was maintained by use of the apparatus described by Johnson and Schneider.[20] We thank the Fisher Scientific Co for a generous gift of chemicals.

General Photooxygenation Procedure. Photooxygenations were run in a 500-ml gas washing bottle in a solution of 250 ml of tetrahydrofuran, 200 ml of distilled water, and 50 ml of pyridine with 10 mg of Methylene Blue as sensitizer. All reactions were run at room temperature with magnetic stirring. The reaction vessel was placed in the center of four General Electric cool white fluorescent lamps (15 W per lamp) and the fluorescent bank was surrounded by reflective aluminum foil. The lights were turned on and oxygen gas, passing through the dispersion disk at the bottom, was continually bubbled through the solution. After completion of the reaction, the tetrahydrofuran was removed by evaporation at reduced pressure. The aqueous layer was extracted several times with diethyl ether and the ether was washed successively with distilled water twice, 200 ml of 2 *N* hydrochloric acid, a solution of aqueous acidified 1 *N* ferrous sulfate, distilled water, saturated sodium bicarbonate solution, distilled water, saturated sodium chloride solution, dried over anhydrous sodium sulfate, and then evaporated to dryness.

Lithium Anion of 9*H*-Pyrrolo[1,2-*a*]indole (7). The lithium anion was prepared in the addition funnel in all experiments. A 10 *M* % excess of a hexane solution of *n*-butyllithium was added by syringe to a magnetically stirred 0.2 *M* solution of 9*H*-pyrrolo[1,2-*a*]indole (**3**) in either anhydrous diethyl ether or anhydrous tetrahydrofuran. The mixture was stirred for 15 min before further reaction, at which time it was a Brunswick green in diethyl ether and a deep red in tetrahydrofuran.

9-Methoxymethyl-9*H*-pyrrolo[1,2-*a*]indole (8). A solution of the anion was prepared from 250 mg (1.6 mmol) of 9*H*-pyrrolo[1,2-*a*]indole (**3**), 1.1 ml (1.76 mmol) of 1.6 *M* *n*-butyllithium, and 8 ml of anhydrous diethyl ether and then slowly added to an ice-cooled mixture of 3.2 g (0.04 mol, 3.01 ml) of chloromethyl methyl ether in 40 ml of anhydrous diethyl ether. The green anion color was discharged immediately upon addition. The mixture was allowed to warm and was stirred at room temperature for 1.5 hr. A white precipitate of lithium chloride formed, was filtered with suction, and was washed with diethyl ether. Thin-layer chromatography on silica gel eluting with methylene chloride indicated a new component with an R_f of 0.46. Evaporation of the solvent yielded a red oil which turned to a glassy black solid within a few seconds. The black material was no longer soluble in ether or other organic solvents.

9-Methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (11). A solution of the anion was prepared from 388 mg (2.5 mmol) of 9*H*-pyrrolo[1,2-*a*]indole (**3**), 1.7 ml (2.72 mmol) of 1.6 *M* *n*-butyllithium, and 12.4 ml of anhydrous tetrahydrofuran and then added to

1.0 ml (1.06 g, 13.3 mmol) of chloromethyl methyl ether in 7.5 ml of anhydrous tetrahydrofuran. Addition of the anion formed a bright orange solution which was immediately photooxygenated. After 2 hr no more 8 could be detected and the reaction mixture was then worked up as previously described. Evaporation of the ether yielded 440 mg of a dark oil, which was chromatographed on an alumina dry column with benzene. Two distinct yellow bands were visible which were cut and the material was eluted with chloroform, yielding 85 mg (16%) of the desired 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**) and 76 mg (18%) of unalkylated 3*H*-pyrrolo[1,2-*a*]indol-3-one (**4**). An analytical sample was prepared by two recrystallizations from hexane to yield 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**) as bright yellow needles: mp 89–90°; ir (chloroform) 2916 (w), 2811 (w), 1723, 1611, 1461, 1377, 1355, 1307, 1131, 1091 (b), 1066 cm^{-1}; uv (ethanol) 221 (ϵ 6100), 269 (8600), 275 sh (8100), 359 (8500) nm; nmr (d_1-chloroform) δ 3.45 (s, 3, CH_3), 4.53 (s, 2, CH_2), 5.93 upfield half of AB quartet (d, 1, J_{1-2} = 6 Hz, C-2), 6.90–7.44 (m, 4, C-1, C-6, C-7, C-8), 7.58–7.75 ppm (m, 1, C-5).

Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.02; H, 5.10; N, 6.49.

The above yields were averaged over 11 separate experiments, in which the alkylated product (**11**) was isolated in 8–24% yield and the unalkylated material (**4**) in 9–35% yield. Stirring the anion for 30 min, increasing the molar ratio of chloromethyl methyl ether to anion, or increasing the concentration of chloromethyl methyl ether failed to alter the yields. Addition of chloromethyl methyl ether to the anion gave a 4.3% yield of alkylated product **11** and a 59% yield of unalkylated material **4.** Photooxygenating for a longer period of time also failed to improve the yield.

9-Benzyloxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (12). A solution of the anion was prepared from 264 mg (1.7 mmol) of 9*H*-pyrrolo[1,2-*a*]indole (**3**) 1.43 ml (1.86 mmol) of 1.3 *M n*-butyllithium, and 8.4 ml of anhydrous tetrahydrofuran and then added to 1.33 g (8.5 mmol) of freshly distilled chloromethyl benzyl ether in 5 ml of anhydrous tetrahydrofuran. The entire reaction mixture was then immediately photooxygenated. After 3 hr no more **9** could be detected and the reaction mixture was then worked up as previously described. Evaporation of the ether yielded 1.25 g of a crude black oil. Chromatography on an alumina dry column and eluting with benzene yielded 225 mg (46%) of a yellow oil which was crystallized by dissolving in a minimum amount of ether and triturating with hexane until a cloudiness persisted. After 4 days in the freezer long yellow needles of **12** were obtained. An analytical sample was prepared by two recrystallizations from ether–hexane: mp 61–63°; ir (chloroform) 3016 (w), 2844 (w), 1724, 1611, 1464, 1358, 1311, 1130, 1090, 1065 cm^{-1}; uv (ethanol) 214 (ϵ 11,000), 270 (5600), 276 sh (5100), 360 (5600) nm; nmr (d_1-chloroform) δ 4.65 (s, 2, CH_2), 4.68 (s, 2, CH_2), 5.98 upfield half of AB quartet (d, 1, J_{1-2} = 6 Hz, C-2), 6.95–7.49 (m, 9, C-1, C-6, C-7, C-8, +5 phenyl protons), 7.65–7.82 ppm (m, 1, C-5).

Anal. Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.73; H, 5.38; N, 4.82.

Maximum yields (42–50%) were obtained by distilling the chloromethyl benzyl ether prior to each reaction. Anhydrous tetrahydrofuran was prepared by distillation from lithium aluminum hydride and stored over sodium. 9*H*-Pyrrolo[1,2-*a*]indole (**3**) was used as pure white needles and dried in a vacuum desiccator prior to use. The molarity of the *n*-butyllithium was checked periodically by the method of Gilman.[4] If these precautions were not taken, the yields dropped to 16–33% and the unalkylated 3*H*-pyrrolo[1,2-*a*]indol-3-one (**4**) was obtained as a side product in 12–24% yield and was isolated as a faster moving component during chromatography of the reaction mixture.

1-Methyl-3a,10b-dihydro-υ-triazolo[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (13b). Pyrrolo[1,2-*a*]indol-3-one (**4**) (120 mg), methyl azide (450 mg), and benzene (0.4 ml) were introduced into a tapered 6-in. test tube. The tube was immersed in a Dry Ice–chloroform bath and sealed with a hot flame. After sealing, the tube was removed from the cold bath and sheathed in a section of flexible rubber tubing as a precaution against an explosion as well as to prevent light from entering. After standing at room temperature for 28 days, the tube was cracked open, excess methyl azide was allowed to evaporate off, and hexane was added to the residue. The crystalline product was collected and washed with hexane until the hexane washings were colorless. The yield of the off-white product, which sintered at 170–175° and melted at 189–192° dec with gas evolution, was 94 mg (59%). One recrystallization from THF–hexane gave pure white crystals which sintered at 190° and melted at 197–198.5° dec (gas evolution): ir (KBr) 5.76 μ; uv (CH_3OH) λ_{max} 208, 241, 268 (shd) and 305 nm (ϵ 5540, 21,800, 9030, and 1750); nmr ($CDCl_3$–DMSO-d_6 (3:2)) δ 3.46 (s, 3, N-CH_3), 5.16 (d, 1, J_{10b-3a} = 10.5 Hz, C-10b, showing apparent additional coupling to C-10, J_{10-10b} = 1 Hz), 5.90 (d, 1, J_{3a-10b} = 10.5 Hz, C-3a), 6.75 (bs, 1, J_{10-10b} = 1 Hz, $W_{1/2}$ = 2 Hz, C-10), 7.27–7.78 (m, 3, C-7, 8, 9), 7.92–8.16 (m, 1, C-6 peri proton).

Anal. Calcd for $C_{12}H_{10}ON_4$: C, 63.70; H, 4.46; N, 24.70. Found: C, 63.80; H, 4.47; N, 24.75.

1-Phenyl-10-methoxymethyl-3a,10b-dihydro-υ-triazolo-[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14a). A solution of 120 mg (0.56 mmol) of 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**), 360 mg (3.03 mmol) of phenyl azide, and 0.72 ml of spectral grade benzene was heated at 75° in a flask covered with aluminum foil. After 24 hr the reaction mixture had become black. The mixture was cooled and evaporated to dryness yielding a crude black solid. The black solid was washed several times with hexane yielding 30 mg (16%) of crude brown material, mp 149–156°, with apparent gas evolution. The crude solid was chromatographed on a silica gel preparative thin layer plate eluting three times with chloroform. A fluorescent band 2–4 cm above the origin was removed and the product was eluted from the silica gel with chloroform. Evaporation of the solvent yielded 18 mg (9.6%) of a tan oil which was crystallized from chloroform–hexane. Four recrystallizations from chloroform–hexane yielded 6 mg (3.2%) of phenyl triazoline (**14a**) as white crystals, mp 150–151°, with apparent gas evolution: ir (chloroform) 2913, 2839, 1756, 1622, 1606, 1461, 1383, 1356, 1317, 1136, 1088 (br), 1064, 1034, 1010, 911 cm^{-1}; uv (cyclohexane) 243 (ϵ 24,000), 276 sh (15,300), 295 sh (11,000) nm; nmr (d_1-chloroform) δ 3.31 (s, 3, CH_3), 4.36 (s, 2, CH_2), 5.70 and 5.93 (AB quartet, 2, J_{10b-3a} = 10.5 Hz, C-10b, C-3a), 7.08–7.65 (m, 8, C-7, C-8, C-9 + phenyl protons), 8.01–8.18 ppm (m, 1, C-6).

1-Benzyl-10-methoxymethyl-3a,10b-dihydro-υ-triazolo-[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14b). A solution of 100 mg (0.47 mmol) of 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**), 333 mg (2.5 mmol) of benzyl azide, and 1.2 ml of spectral grade benzene was heated at 75° for 20 hr in a flask covered with aluminum foil. The reaction mixture was cooled and triturated with hexane yielding a brown solid. The solid was washed several times with hot hexane to remove the unreacted starting material yielding 46 mg of crude brown triazoline (**14b**), mp 143–147°, with apparent gas evolution. The hexane washings were chromatographed on an alumina dry column eluting with chloroform. Two distinct bands were visible; a broad yellow band of starting material (**11**) with an R_f of 0.50–0.75 followed by a narrow brown band of benzyl triazoline (**14b**) with an R_f of 0.31. The bands were cut and the material was eluted with chloroform yielding 45 mg of unreacted starting material (**11**) and an additional 23 mg of product giving a total yield of 69 mg (42% yield, 77% conversion) of benzyl triazoline (**14b**). An analytical sample was prepared by three recrystallizations from ethyl acetate to yield 22 mg (14% yield, 25% conversion) of benzyl triazoline (**14b**) as white needles, mp 158–159°, with apparent gas evolution: ir (chloroform) 2977 (w), 2911 (w), 1755, 1633, 1461, 1383, 1322, 1135, 1087 (br) cm^{-1}; uv (ethanol) 209 (ϵ 9300), 244 (13,800), 270 sh (6700), 309 sh (1400) nm; nmr (d_1-chloroform) δ 3.46 (s, 3, CH_3), 4.53 (s, 2, CH_2), 4.86 and 5.31 (AB quartet, 2, J_{AB} = 16 Hz, benzyl CH_2), 4.96 and 5.81 (AB quartet, 2, J_{10b-3a} = 10.5 Hz C-10b, C-3a), 7.20–7.65 (m, 8, C-7, C-8, C-9 + 5 phenyl protons), 8.02–8.18 ppm (m, 1, C-6).

Anal. Calcd for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.17. Found: C, 69.24; H, 5.29; N, 16.19.

1-Benzyl-10-benzyloxymethyl-3a,10b-dihydro-υ-triazolo-[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14f). A solution of 325 mg (1.12 mmol) of 9-benzyloxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**12**), 300 mg (2.25 mmol) of benzyl azide, and 1.0 ml of spectral grade benzene was heated at 76–77° for 63 hr. The mixture was cooled and triturated with hexane to crystallize the product. The solid was washed with hexane to remove the unreacted starting material yielding 336 mg (71%) of crude brown triazoline (**14f**). The hexane washings were chromatographed on a silica gel PF preparative thin layer plate eluting with chloroform yielding 22 mg (7%) of recovered 9-benzyloxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**12**). The crude triazoline (**14f**) was recrystallized twice from ethyl acetate to yield 220 mg (47% yield, 50% conversion) of pure product. An analytical sample was prepared by two additional recrystallizations from ethyl acetate to yield benzyl triazoline (**14f**), as white crystals, mp 165–166° with apparent gas evolution: ir (chloroform) 2914 (w), 2847 (w), 1758, 1628, 1464, 1391, 1364, 1325, 1134, 1086, 1067 cm^{-1}; uv (ethanol) 243 (ϵ 17,100), 271 sh (7900), 304 sh (1700) nm; nmr (d_1-chloroform) δ 4.59 (s, 2, CH_2), 4.63 (s, 2, CH_2), 4.82 and 5.25 (AB quartet, 2, J_{AB} = 16 Hz, benzyl CH_2), 4.91

and 5.82 (AB quartet, 2, J_{10b-3a} = 10.5 Hz, C-10b, C-3a), 7.13–7.57 (m, 13, C-7, C-8, C-9 + 10 phenyl protons), 8.02–8.18 ppm (m, 1, C-6).

Anal. Calcd for $C_{26}H_{22}N_4O_2$: C, 73.92; H, 5.25; N, 13.26. Found: C, 73.79; H, 5.35; N, 13.27.

1,10-Bis(methoxymethyl)-3a,10b-dihydro-*v*-triazolo[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14e). A solution of 48 mg (0.23 mmol) of 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**), 132 mg (1.5 mmol) of methoxymethyl azide, and 0.6 ml of spectral grade benzene was heated at 75° for 7 days under an atmosphere of argon. The reaction mixture was cooled and triturated with hexane yielding brown crystals. The crystals were washed several times with hexane to remove the unreacted starting material yielding 31 mg of crude brown triazoline (**14e**). The hexane washings were chromatographed on a silica gel dry column eluting with methylene chloride. Two bands were visible, a broad yellow band of starting material followed by a narrow brown band of triazoline. The bands were cut and the material was eluted with chloroform yielding 11 mg of unreacted 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**) and an additional 7 mg of product giving a total yield of 38 mg (55% yield, 75% conversion) of crude triazoline (**14e**). An analytical sample was prepared by three recrystallizations from ethyl acetate yielding 11 mg (16% yield, 22% conversion) of methoxymethyl triazoline (**14e**) as light brown needles, mp 158–160° with apparent gas evolution: ir (chloroform) 2989, 2928, 2822, 1761, 1639, 1489, 1472, 1389, 1366, 1328, 1316, 1136, 1094, 1071, 1010, 988, 910 cm^{-1}; uv (ethanol) 241 (ϵ 15,000), 295 (1600), 305 (1400) nm; nmr (d_1-chloroform) δ 3.35 (s, 3, CH_3), 3.55 (s, 3, CH_3), 4.71 (s, 2, CH_2), 5.27 (s, 2, CH_2), 5.29 and 5.96 (AB quartet, 2, J_{10b-3a} = 10.5 Hz, C-10b, C-3a), 7.30–7.68 (m, 3, C-7, C-8, C-9), 8.03–8.20 ppm (m, 1, C-6).

Anal. Calcd for $C_{15}H_{16}N_4O_3$: C, 59.99; H, 5.37; N, 18.66. Found: C, 59.87; H, 5.46; N, 18.60.

1-Methyl-10-methoxymethyl-3a,10b-dihydro-*v*-triazolo-[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14c). A solution of 100 mg (0.47 mmol) of 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**), 0.4 ml of spectral grade benzene, and approximately 0.5 ml of freshly prepared methyl azide was sealed in a test tube, which was protected with a rubber sleeve against possible explosion. The tube was allowed to stand at room temperature for 19 months.[19] The tube was opened and the methyl azide was allowed to evaporate. Removal of the benzene yielded 108 mg (85%) of a crude brown solid which was washed with cold ethyl acetate yielding 32 mg (25%) of light tan crystals of methyl triazoline (**14c**). The ethyl acetate washings were chromatographed on a silica gel PF preparative thin layer plate eluting with ethyl acetate. A fluorescent band with an R_f of 0.67 was removed and the material was eluted from the silica gel with chloroform yielding an additional 38 mg of product giving a total yield of 70 mg (55%) of methyl triazoline (**14c**). An analytical sample was prepared by preparative thin-layer chromatography on a silica gel G prep plate eluting with 2:1 chloroform:ethyl acetate. A fluorescent band 3–5 cm from the origin was cut and the product was eluted from the silica gel with chloroform. Evaporation of the solvent yielded methyl triazoline (**14c**) as white needles, mp 146–147°, with apparent gas evolution: ir (chloroform) 2989, 2922, 1755, 1633, 1460, 1383, 1322, 1169, 1135, 1091, 1013, 987, 921 cm^{-1}; uv (ethanol) 241 (ϵ 21,000), 270 sh (8600), 295 sh (2400), 305 sh (2000) nm; nmr (d_1-chloroform) δ 3.53 (s, 3, CH_3), 3.57 (s, 3, CH_3), 4.74 (s, 2, CH_2), 5.04 and 5.84 (AB quartet, 2, J_{10b-3a} = 10.5 Hz, C-10b, C-3a), 7.27–7.63 (m, 3, C-7, C-8, C-9), 8.05–8.22 ppm (m, 1, C-6).

Anal. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 61.88; H, 5.39; N, 20.40.

1-Benzyloxymethyl-10-methoxymethyl-3a,10b-dihydro-*v*-triazolo[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (14d). A solution of 84 mg (0.39 mmol) of 9-methoxymethyl-3*H*-pyrrolo[1,2-*a*]indol-3-one (**11**), 330 mg (2 mmol) of benzyloxymethyl azide, and 1.0 ml of spectral grade benzene was heated at 75° for 4 days. The reaction mixture was cooled and evaporated to dryness yielding a crude dark oil which was chromatographed on silica gel G preparative thin layer plates with methylene chloride, giving a tan oil which was crystallized from chloroform–hexane yielding 85 mg (58%) of light brown crystals. An analytical sample was prepared by two recrystallizations from chloroform–hexane to yield 60 mg (41%) of light tan crystals of benzyloxymethyl triazoline (**14d**), mp 126–128° with apparent gas evolution: ir (chloroform) 3000, 2922, 2394, 1750, 1633, 1511, 1478, 1461, 1422, 1378, 1316, 1311, 1130, 1087, 1056, 1007, 919 cm^{-1}; uv (ethanol) 240 (ϵ 23,900), 268 sh (9700), 298 (2500), 304 (2500) nm; nmr (d_1-chloroform) δ 3.53 (s, 3, CH_3), 4.56 (s, 2, CH_2), 4.65 (s, 2, CH_2), 5.20 and 5.79 (AB quartet, 2, J_{10b-3a} = 11 Hz, C-10b, C-3a), 5.40 (s, 2, CH_2), 7.24–7.67 (m, 8, C-7, C-8, C-9 + 5 phenyl protons), 8.00–8.18 ppm (m, 1, C-6).

Anal. Calcd for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.88. Found: C, 67.02; H, 5.34; N, 14.87.

1a,8b-Dihydro-1-benzylazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indol-2(1*H*)-one (19). A solution of 77 mg (0.25 mmol) of **13a**, 10 ml of freshly distilled piperylene, and 150 ml of freshly distilled 95% ethanol was placed in a water-cooled (15°) photolysis apparatus. After purging with argon for 20 min, the stirred solution was irradiated with a medium pressure mercury arc lamp (Hanovia, 450 W, Pyrex filter) for 2.5 hr. The crude product was absorbed onto 1 g of dry-column silica gel and placed atop a column of the same absorbant (33 × 3.8 cm). The column was eluted with chloroform, the band 10.5 to 14 cm below the top of the column being separated. Work-up of this band yielded 20 mg (29%) of a pale yellow oil. The oil was taken up in ether and after chilling at 0° for several days it gave white crystals: mp 121–123°; ir (KBr) 5.74 μ; uv (MeOH) λ_{max} 218, 249, 310 nm (ϵ_{max} 5480, 15,700, and 2140); nmr ($CDCl_3$) δ 3.17, 3.38 (AB quartet, J_{8b-1a} = 4.3 Hz, C-8b, C-1a), 3.73 (bs, 2, $W_{1/2}$ = 2 Hz, benzylic CH_2), 6.50 (bs, 1, W 1/2 = 2.5 Hz, C-8), 7.17–7.67 (m, 8, C-5, 6, 7 + 5 phenyl protons), 7.92–8.02 (m, 1, C-4); *m/e* calcd for $C_{18}H_{14}N_2O$, 274.1106, and found, 274.1138.

8-Methoxymethyl-1a,8b-dihydro-1-phenylazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indol-2(1*H*)-one (20a). A solution of 15 mg (0.05 mmol) of 1-phenyl-10-methoxymethyl-3a,10b-dihydro-*v*-triazolo[4′,5′:3,4]pyrrolo[1,2-*a*]indol-4(1*H*)-one (**14a**) and 140 ml of freshly distilled benzene was placed in a photochemical reaction vessel equipped with a water-cooled immersion well. The reaction vessel was covered in the back with reflective foil. The solution was purged with nitrogen for 15 min prior to irradiation with a Sears-Roebuck sun lamp No. 7081 held 2.5 cm from the reaction vessel through two thicknesses of plate glass. The solution was irradiated for 15 min and then evaporated to dryness yielding 14 mg (100%) of a brown oil which was crystallized from chloroform–hexane. Attempts at purification by preparative chromatography on silica gel or alumina were unsuccessful. Three recrystallizations from chloroform–hexane yielded 7 mg (50%) of phenyl aziridine (**20a**) as a light tan solid: ir (chloroform) 3000, 2922, 2844, 1744, 1639, 1600, 1494, 1461, 1378, 1133, 1093, 1019, 924 cm^{-1}; nmr (d_1-chloroform) δ 3.59 (s, 3, CH_3), 3.85 and 4.20 (AB quartet, 2, J_{8b-1a} = 3.4 Hz, C-8b, C-1a), 4.78 (s, 2, CH_2), 6.93–7.67 (m, 8, C-5, C-6, C-7 + 5 phenyl protons), 7.73–7.92 ppm (m, 1, C-4).

8-Methoxymethyl-1a,8b-dihydro-1-benzylazirino[2′,3′:3,4]pyrrolo[1,2-*a*]indol-2(1*H*)-one (20b). A solution of 42 mg (0.12 mmol) of 1-benzyl-10-methoxymethyl-3a,10b-dihydro-*v*-triazolo[4′,5′:3,4]pyrrolo]1,2-*a*]indol-4(1*H*)-one (**14b**), 10 ml of freshly distilled piperylene, and 150 ml of freshly distilled benzene was placed in a photochemical reaction vessel equipped with a water-cooled quartz immersion well. The solution was purged with nitrogen for 15 min prior to irradiation with a Hanovia 679A-36 high pressure quartz mercury-vapor lamp (450 W) through a 2-mm Pyrex filter sleeve. Photolysis was stopped after 1.5 hr even though the starting triazoline had not been completely consumed. Evaporation of the reaction mixture yielded 66 mg of a crude brown oil. Oil (11 mg) was chromatographed on silica gel PF preparative thin layer plate eluting three times with chloroform. A bright orange band was visible with an R_f of 0.25 and a fluorescent band with an R_f slightly less. The bands were removed and the material was eluted from the silica gel with chloroform. The lower band proved to be recovered starting triazoline (**14b**) by ir and comparative thin layer chromatography with authentic material. The orange band yielded 4 mg of an oil whose ir exhibited the desired carbonyl. The remainder of the plate failed to yield any components whose ir contained a carbonyl absorption. The remaining 55 mg of crude reaction mixture was chromatographed similarly. Isolation of the desired component yielded an additional 10 mg giving a total yield of 14 mg (36%) of a crude oil which was crystallized from ether–hexane. The crystals were washed once with cold diethyl ether to remove the dark color. Two recrystallizations from ether–hexane yielded 7 mg (18%) of benzyl aziridine (**20b**): mp 108–111°; ir (chloroform) 3000, 2917, 2839, 1750, 1639, 1461, 1378, 1311, 1133, 1091, 1030 cm^{-1}; nmr (d_1-chloroform) δ 3.18 and 3.48 (AB quartet, 2, J_{8b-1a} = 4.5 Hz, C-8b, C-1a), 3.33 (s, 3, CH_3), 3.36 and 3.71 (AB quartet, 2, J_{AB} = 8 Hz, benzyl CH_2), 4.63 (s, 2, CH_2), 7.22–7.63 (m, 8, C-5, C-6, C-7 + 5 phenyl protons), 7.88–8.07 ppm (m, 1, C-4); *m/e* calcd for $C_{20}H_{18}N_2O_2$, 318.1368, and found, 318.1340.

8-Benzyloxymethyl-1a,8b-dihydro-1-benzylazirino[2′,3′:3,4]pyrrolo[1,2-*a*]-indol-2(1*H*)-one (20c). A solution of 209 mg (0.5 mmol) of 1-benzyl-10-benzyloxymethyl-3a,10b-dihydro-*v*-triazolo[4′,5′:3,4]pyrrolo[1,2-a]indol-4(1*H*)-one (**14f**), 10 ml of

freshly distilled piperylene, and 150 ml of freshly distilled benzene was placed in a photochemical reaction vessel equipped with a water-cooled quartz immersion well. The solution was purged with nitrogen for 15 min prior to irradiation with a Hanovia 679A-36 high pressure quartz mercury-vapor lamp (450 W) through a 2-mm Pyrex filter sleeve. The photolysis was stopped after 6 hr even though the starting triazoline had not been completely consumed. Evaporation of the reaction mixture yielded 418 mg of a dark orange oil, which was chromatographed on a silica gel. Early fractions afforded 45 mg of product; intermediate fractions contained both aziridine and starting triazoline. Later fractions yielded 78 mg of recovered triazoline (**14f**). The impure product was chromatographed on silica gel preparative thin layer plates eluting each three times with chloroform. A broad orange band approximately 5 cm above the origin was visible. The band was removed and the product was eluted from the silica gel with chloroform. Evaporation of the solvent yielded 26 mg of an oil, which was crystallized from ether–hexane. Two recrystallizations from ether–hexane yielded 10 mg (5.1% yield, 8.2% conversion) of benzyl aziridine (**20c**) as light tan crystals; mp 84–85°; ir (chloroform) 2983, 2844, 1744, 1639, 1461, 1389, 1361, 1306, 1136, 1091, 1071, 1028, 921 cm^{-1}; nmr (d_1-chloroform) δ 3.10 and 3.39 (AB quartet, 2, J_{8b-1a} = 4.5 Hz, C-8b, C-1a), 3.60 and 3.66 (lines 2 and 3 of apparent AB quartet, 2, benzyl CH_2), 4.49 (s, 2, CH_2), 4.68 (s, 2, CH_2), 6.68–7.52 (m, 13, C-5, C-6, C-7 + 10 phenyl protons), 7.66–7.99 ppm (m, 1, C-4); *m/e* calcd for $C_{26}H_{22}N_2O_2$, 394.1681, and found, 394.1643.

1-(*N*-Formyl-*N*-phenyl)amino-2-diazo-3*H*-pyrrolo[1, 2-*a*]-indol-3-one (15). To a 50-ml round-bottomed flask containing 4 ml of *N,N*-dimethylformamide (DMF) at 5° was added dropwise 100 mg (0.65 mmol) of phosphorous oxychloride. The resulting solution was allowed to stand for 10 min before a solution of 155 mg (0.54 mmol) of **5** in 4 ml of DMF was introduced over a period of 3 min. The solution was stirred at 5°C for 1 hr, during which time the color changed from an initial pale yellow to a yellow-orange. The contents of the flask were then poured into ice and water and extracted with ether. The ether layer was discarded. The aqueous layer was then made slightly basic by the addition of 2 *N* NaOH and again extracted with ether. The yellow ether layer was washed twice with water, dried over magnesium sulfate, filtered, and evaporated to dryness. The crude yield was 160 mg (84%) of light brown crystals which after two recrystallizations from THF–hexane and one from ethyl acetate gave analytically pure light yellow crystals, mp 173–76° dec, followed by gas evolution at 178°: ir ($CHCl_3$) 3.33, 4.20, 4.78, 5.82,5.99 μ; uv (MeOH) λ_{max} 220, 268, 308 nm (ϵ_{max} 12,280, 17,840, 8000); nmr ($CDCl_3$) δ 6.90 (bs, 1, $W_{1/2}$ = 2.5 Hz, C-9), 7.30–8.10 (m, 9, C-1, 6, 7, 8 + 5 phenyl protons), 8.23–8.50 (m, 1, C-5), 8.93 (s, 1, NCHO).

Anal. Calcd for $C_{18}H_{12}O_2N_4$: C, 68.35; H, 3.82; N, 17.71; mass spectrometer, 316.0960. Found: C, 68.49; H, 3.81; N, 17.88; mass spectrometer, 316.0976.

Registry No.—**3,** 247-66-5; **4,** 24009-76-5; **5,** 24009-77-6; **7,** 52827-13-1; **8,** 52827-14-2; **11,** 52827-15-3; **12,** 52827-16-4; **13a,** 26709-66-0; **13b,** 52827-17-5; **14a,** 52856-34-5; **14b,** 52856-35-6; **14c,** 52827-18-6; **14d,** 52827-19-7; **14e,** 52827-20-0; **14f,** 52827-21-1; **15,** 52827-22-2; **19,** 52827-23-3; **20a,** 52827-24-4; **20b,** 52827-25-5; **20c,** 52827-26-6; chloromethyl methyl ether, 107-30-2; chloromethyl benzyl ether, 3587-60-8; methyl azide, 624-90-8; phenyl azide, 622-37-7; benzyl azide, 622-79-7; methoxymethyl azide, 52827-27-7; benzyloxymethyl azide, 52827-28-8; piperylene, 504-60-9.

References and Notes

(1) (a) We gratefully acknowledge the financial support of the U.S. Public Health Service, Grant CA 11421. (b) Taken from the Ph.D. Theses of R.J.K. and G.J.S., Fordham University, 1974. (c) Presented in part at the 6th Northeast Regional Meeting of the American Chemical Society, Burlington, Vt., August 1974, Paper No. 174.

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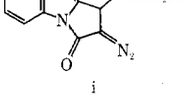

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