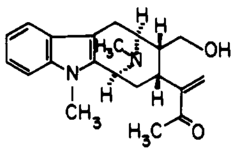
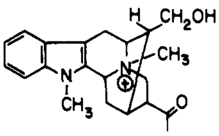
approaches give impetus to biomimetic syntheses of these alkaloids. In previous work in our laboratory,[3] macroline (**1**) was shown to serve as a direct precursor of the bisindole alkaloids villalstonine, alstonisidine, macralstonine, and macralstonidine as well as of the monomeric base alstonerine and, by extension, alkaloids in the talcarpine series.



1

Macroline (**1**) itself has not been encountered as a natural product, which led us to propose[3] that it or an equivalent such as the β-ketoammonium salt (**2**), which would arise from a sarpagine-like structure, exists in low, steady-state concentrations on the biosynthetic pathways. We now report a synthesis of macroline (**1**) via a derivative of **2** which gives strong support for this biogenetic proposal.



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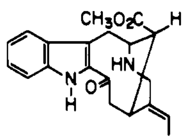

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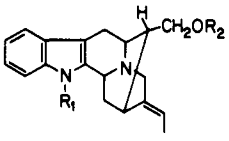
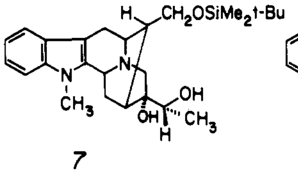


4 $R_1 = R_2 = H$
5 $R_1 = H, R_2 = SiMe_2t\text{-}Bu$
6 $R_1 = Me, R_2 = SiMe_2t\text{-}Bu$



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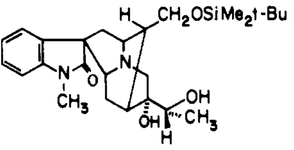

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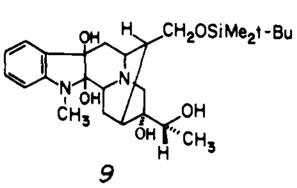

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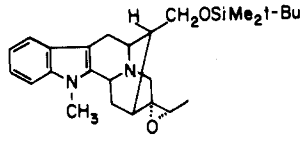

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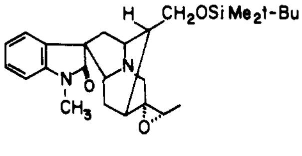

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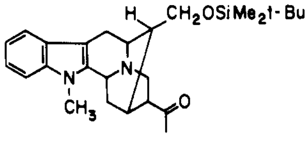

12

Perivine (**3**) was converted to normacusine B (**4**) by methods close to those previously reported.[4] The primary hydroxyl group of **4** was protected as the *tert*-butyldimethylsilyl ether **5**[5] (t-BuMe$_2$SiCl, imidazole, DMF), then converted to the N_a-methylated compound **6** (KH, NH_3/THF, MeI). Attempts to epoxidize the ethylidene double bond directly, with selectivity and in high yield, in the presence of the indole nucleus and tertiary nitrogen, either via hydroxyl-directed reagents[6] on normacusine B (**4**) or with other epoxidizing reagents on the silyl ether **6**, were unsuccessful.[7] However, osmylation of **6** (1.1 equiv of OsO_4 in THF/py, sodium metabisulfite workup) gave an inseparable mixture of the diol **7** and the spirooxindole **8**, the latter presumably arising from the tetrol **9** during chromatography of the crude mixture. The osmylation proceeded stereoselectively owing to the bulky *tert*-butyldimethylsilyl function blocking one side of the ethylidene group. The mixed diols **7** and **8** were tosylated (TsCl, py) and the tosylates converted to the epoxides **10** and **11** with NaH/THF. The desired epoxide **10** (one stereoisomer) could be separated cleanly by direct crystallization. Rearrangement of **10** (freshly prepared $MgBr_2$, refluxing Et_2O/benzene) gave the oily ketone **12** which with Me_2SO_4/K_2CO_3 (refluxing benzene, 18 h) followed by $Bu_4N^+F^-$ (THF/H_2O) gave only macroline (**1**), identical in all respects with material obtained by degradation of villalstonine.[8]

This work gives direct in vitro experimental support to the biogenetic hypothesis proposed earlier,[3] and implies that sarpaginelike structures such as normacusine B (**4**) are the precursors of all the macroline-related indole alkaloids.

Acknowledgment. We are very grateful to Dr. Gerald L. Thompson, Lilly Research Laboratories, for generous gifts of perivine.

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(2) For a general review of this topic, see: Dalton, D. R. "The Alkaloids"; Marcel Dekker: New York, 1979; pp 432–479.

(3) Garnick, R. L.; Le Quesne, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 4213, and references cited therein.

(4) Gorman, M.; Sweeney, J. *Tetrahedron Lett.* **1964**, 3105.

(5) All new compounds gave satisfactory analytical and spectral data.

(6) See, for example: Sharpless, K. B.; Michaelson, C. R. *J. Am. Chem. Soc.* **1973**, *95*, 6136.

(7) See, for example: Kutney, J. P.; Balserich, J.; Bokelman, G. H.; Hibino, T.; Honda, T.; Itoh, I.; Ratcliffe, A. H.; Worth, B. R. *Can. J. Chem.* **1978**, *56*, 62. Mimoun, H.; Seree de Roch, I.; Sajus, L. *Tetrahedron* **1970**, *26*, 37.

(8) Hesse, M.; Hürzeler, H.; Gemenden, C. W.; Joshi, B. S.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1965**, *48*, 689.

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Use of Holography to Investigate Photochemical Reactions

Sir:

In order to monitor a photochemical reaction, it is necessary in some way to measure the disappearance of the reactants or the appearance of the products. A variety of techniques have been developed to accomplish this.[1] In perhaps the most frequently used technique, one follows changes in optical absorption of the reactants or products. The sensitivity of this kind of experiment is low because of the difficulties involved in detecting small absorption changes. Here, a new technique is described that allows one, in a very simple manner, to follow the course of the reaction by measuring the growth in intensity of a holographic image. This method is essentially a zero-background technique and has the high sensitivity characteristic of techniques of this type. Furthermore, since the intensity of the hologram depends not only on changes in the absorption coefficient but also on changes in

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(1) Calvert, J. G.; Pitts, J. N. "Photochemistry"; Wiley: New York, 1966; pp 580–670.

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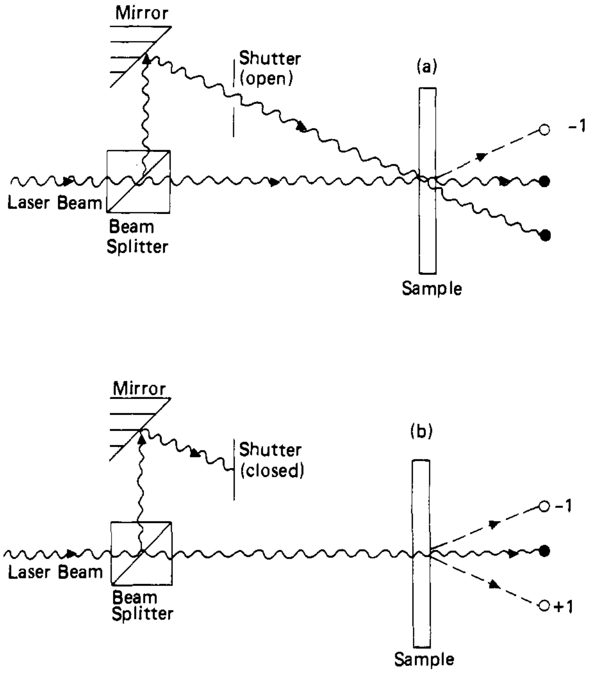

Figure 1. Diagram of the production of photochemical holograms. The wavy line in both cases represents the path of the laser beam and the dotted line the path of the deflected holographic beam. Open circles represent the holographic image and blackened circles the original laser beam. (a) The setup for writing a hologram. (b) The setup for reading the hologram.

the index of refraction, it can be observed in wavelength regions where there is no product absorption or where product and reactant absorptions overlap. The technique should be useful where the reaction being investigated can occur in a solid phase such as in polymer, glass, or crystalline matrixes.

The principle of the holographic method is illustrated in Figure 1. Coherent light from a laser is divided by a beam splitter into two beams. The laser may be repetitively pulsed or CW; in the example described here, a CW Ar$^+$ laser was used. The divided laser beam is recombined and focused in the sample where interference fringes are produced (Figure 1a). If photochemistry is induced by radiation at the laser wavelength, then the fringe pattern is permanently fixed in the medium by the consequent changes in absorption intensity and index of refraction.[2] Since only the change in index of refraction and absorption intensity is important, the technique can be used when a small concentration of a photoreactive compound with a large extinction coefficient is being studied. This technique measures the accumulated photochemical change and thus differs from the transient hologram technique that has previously been utilized to measure excited-state transport properties and lifetimes.[3] It should also be noted that photochemical systems have previously been investigated for use as holographic materials.[4]

One of the two beams is blocked to read the hologram (Figure 1b). A fraction of the intensity of the reading beam is deflected by the grating-like interference fringes and forms a replica of the blocked beam. This holographic image is called the +1 image. Another image, the −1 image, occurs on the opposite side of the reading beam. In the experiments reported here, a photodiode was placed at the location of the −1 image, and the growth of the hologram was continuously monitored by following the growth of this image. Scattering of the laser light within the solid matrix reduces the sensitivity of the technique, and it is desirable to use matrixes of reasonable optical quality.

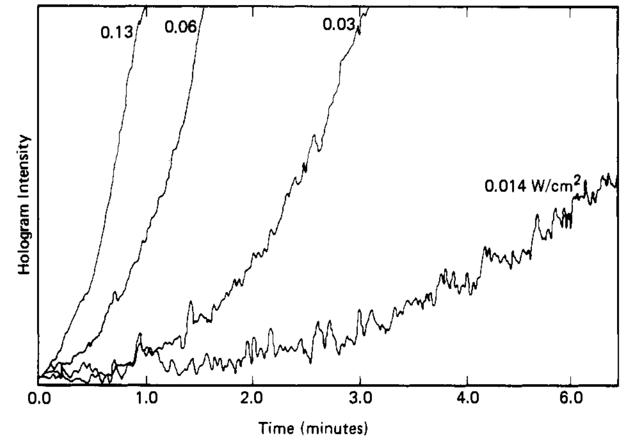

Figure 2. Growth curves for camphorquinone in polyvinylcarbazole by using the 488-nm line of an Ar$^+$ laser.

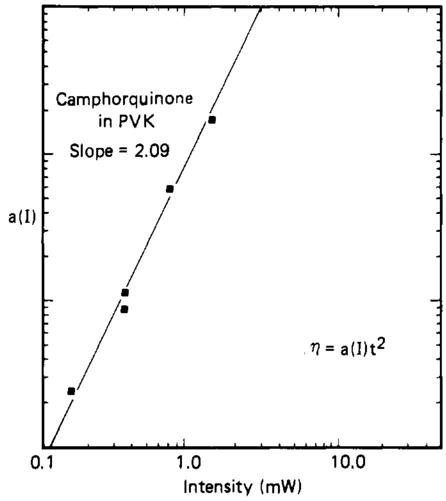

Figure 3. Plot of the parameter $a(I)$ vs. the laser intensity.

The intensity of a hologram is expressed in terms of its efficiency, η. The efficiency is the light intensity deflected into the holographic image divided by the incident light intensity. Using the theory of Kogelnik,[5] it can be shown that, regardless of the optical density of the sample to the exposing wavelength, the parameter η is accurately described during the initial portion of the growth of the hologram by where $a(I) = bI^{2n}$ and t is the

$$\eta = a(I)t^2 \qquad (1)$$

exposure time, I the laser intensity, and n the order (required number of absorbed photons per molecule dissociated) of the photochemical reaction. b depends on the frequency of the laser light and is proportional to the absorption coefficient and photochemical quantum yield. Measurements of the intensity dependence of η thus yield the order of the photochemical reaction. One can measure the wavelength dependence of b by using a slightly different setup. A knowledge of the absorption coefficient of the reactant then enables one to obtain the wavelength dependence of the relative quantum yield for one-photon processes.

As a specific example of the use of the holographic technique, the photoreaction of camphorquinone (CQ) in polyvinylcarbazole (PVK) is treated. Although the details of this reaction are not known, it is believed to involve excited-state intermolecular hy-

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(2) Nussbaum, A.; Phillips, R. A. "Contemporary Optics for Scientists and Engineers"; Prentice-Hall: Englewood Cliffs, NJ, 1976; pp 303–317.

(3) Eichler, H. J. *Opt. Acta* **1977**, *24*, 631.

(4) Tomlinson, W. J.; Chandross, E. A.; Fork, R. L.; Pryde, C. A.; Lamola, A. A. *Appl. Opt.* **1972**, *11*, 533. Bartolini, R. A.; Bloom, A.; Weakliem, H. A. *Ibid.* **1976**, *15*, 1261.

(5) Kogelnick, H. *Bell Syst. Tech. J.* **1969**, *48*, 2909. Bjorklund, G. C.; Burland, D. M., unpublished results.

drogen atom abstraction.[6] Growth curves of η vs. time are shown for CQ in Figure 2. The temporal dependence is quadratic as described by eq 1. In Figure 3 , the quantity $a(I)$ which has been extracted from the growth curves is shown as a function of I. From the slope of this curve, one obtains a value of $n = 1.04$, indicating that the reaction is a linear single-photon process. The accuracy of the determination of n by this method is much greater than by the conventional method of following the decrease in the absorption intensity of the starting material.[7] The uncertainty in values of n obtained by the holographic technique is 5% compared with 20% for the direct absorption method. The holographic technique has the additional advantage that only a tiny portion of each sample, i.e., the area of the focused laser beam (<0.5 mm^2), is used for each measurement.

In summary, a simple new method of following the temporal course of a photochemical reaction has been described. The technique does not require sophisticated optics or electronics.

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(6) Meinwald, J.; Klingele, H. O. *J. Am. Chem. Soc.* **1966,** *88,* 2071. Bloom, A.; Bartolini, R. A.; Ross, D. L. *Appl. Phys.* Lett. **1974,** *24,* 612. Bartolini, R. A.; Bloom, A.; Escher, J. S. *Ibid.* **1976,** *28,* 506.

(7) Murai, H.; Obi, K. *J. Phys. Chem.* **1975,** *79,* 24446. Burland, D. M.; Haarer, D. *IBM J. Res. Dev.* **1979,** *23,* 534.

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Direct Cyanation of Aromatics

Sir:

We wish to report a method for the direct introduction of a cyano group onto aromatic rings. Since there are no general methods for direct cyanation,[1] this reaction may have synthetic utility. The results are of particular interest because they illustrate an unusual preparative approach—plasma chemistry.[2] Furthermore, the observed positional selectivity patterns, which include *ipso substitution for all substituents examined,* are exceptional and of considerable intrinsic interest.

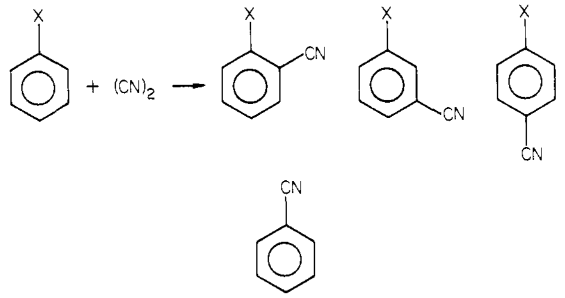
The inductively coupled plasma apparatus is very similar to those previously described.[3,4] Cyanogen (Matheson Co.) and the respective aromatic compound were codistilled through the discharge zone generated by a rf generator at 13.56 MHz. Products and unreacted starting materials were frozen out in a liquid nitrogen cooled trap and were analyzed by GLC. The products were identified by comparison with authentic samples and in most cases confirmed by GLC-MS. Yields were generally estimated by GLC with an internal standard.

Consider first the conversion of benzene to benzonitrile. Under appropriate flow rate and power conditions, the yield of benzonitrile is 94% based upon the 45% benzene (8 g) which reacted during one pass. The yield based on reacted cyanogen is 64%. A wide variety of substituted benzenes (C_6H_5X, X = CH_3, CF_3, OH, F, Cl, Br) and pyridine are similarly cyanated, providing good yields of ortho, meta, para, and ipso-substituted products.

Table I. Yields of Cyanoaromatics from C_6H_5X

		flow rate, mmol min^{-1}		% yield[b] of phenyl derivative			
X	power, W	r_A[a]	r_B[a]	o-X, CN	m-X, CN	p-X, CN	CN
H	45	4.3	2.9	1.9[c]	2.8[c]	1.7[c]	94
CH_3	70	5.8	3.2	26	21	13	11
CF_3	48	2.1	2.0	11	32	9.1	6.0
OH	48	2.1	1.5	18	10	8.3	9.0
F	40	3.3	1.8	14	17	14	4.0
Cl	50	2.5	1.9	17	19	17	20
Br	60	2.6	1.7	5.3	6.2	4.2	9.2
N[d]	50	4.0	1.2	20	34	10	

[a] r_A and r_B are flow rates of cyanogen and the respective aromatic compound. [b] Yields based on reacted aromatics and are representative of several runs. Conversion was ~70% of the cyanogen and ~50% of the aromatic. [c] Dicyanobenzenes. [d] Starting material is pyridine.



Typical yields are indicated in Table I. In these experiments the conversion of aromatic was typically 50% and the conversion of cyanogen was typically 70%. Only in the case of benzene were the yields optimized. Hydrogen cyanide was always found as a coproduct, and small amounts of dicyanoaromatics were also produced. These products were minimized by keeping the conversion of aromatic reactant less than 60%. In all reactions, not more than 0.5% biphenyl was found. For toluene, less than 0.2% benzyl cyanide from side-chain reaction was observed and about 5% bibenzyl was detected.

The utility of this reaction is limited by the unselectivity of substitution and the need to vaporize the aromatic.[5] The advantages are that the reaction involves no heating, solvent or catalyst and a flow system. This is one of a very few cases in which two compounds have been used for a reaction *in the plasma zone,*[4-7] and to our knowledge the only one which gives clean products for several substrates.

The observation that ipso substitution competes with substitution for hydrogen is unusual.[8] The generality of ipso substitution is unprecedented, and especially remarkable is the displacement of fluoro. We suspect that the positional selectivity results from a very exothermic addition of cyano radical to the aromatic, followed by immediate loss of a hydrogen atom or the substituent, before the activated product can lose its energy by collisions. The mechanism, the origin of the selectivity, and other aspects will be elaborated in a future publication.

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(1) Methods for the direct replacement of aromatic hydrogen by cyano are (a) Electrolysis of methoxyaromatics and cyanide: S. Andreades and E. W. Zahnow, *J. Am. Chem. Soc.,* **91,** 4181 (1969); K. Yoshida, M. Shigi, and T. Fueno, *J. Org. Chem.,* **40,** 63 (1975). (b) Photolysis of certain aromatics in cyanide solution or in the presence of ICN: E. Havinga and J. Cornelisse, *Pure Appl. Chem.,* **47,** 1 (1976); *Chem. Rev.,* **75,** 353 (1975); S. Nilsson, *Acta Chem. Scand.,* **27,** 329 (1973). (c) Diazotation of cyanamide in the presence of aromatic compounds. L. Everson, S. Nilsson, and B. Rietz, *Acta Chem. Scand.,* **26,** 3870 (1972). (d) Pyrolysis of benzene and cyanogen in the presence of supported metal catalysts. The most recent of these is by Bock et al. H. Bock, B. Solouki, J. Wittman and H.-J. Arpe, *Angew. Chem., Int. Ed. Engl.,* **17,** 933 (1978).

(2) H. Suhr, *Angew. Chem., Int. Ed. Engl.,* **11,** 781 (1972). H. Suhr in "Techniques and Applications of Plasma Chemistry", J. R. Hollahan and A. T. Bell, Eds., Wiley, New York, 1974, Chapter 2.

(3) M. Tezuka and L. L. Miller, *J. Am. Chem. Soc.,* **100,** 4201 (1978).

(4) L. L. Miller and A. B. Szabo, *J. Org. Chem.,* **44,** 1670 (1979).

(5) A similar plasma reaction can be performed by using CH_3CN in place of C_2N_2,[4] but much lower yields for substituted benzenes and competing methylations are problems.

(6) H. Suhr and A. Szabo, *Liebigs Ann. Chem.,* **752,** 37 (1971); H. Suhr and G. Rosskamp, German Patent 2110653; *Chem. Abstr.,* **77,** 151642b (1972).

(7) R. J. Lagow, L. L. Gerchman, R. A. Jacob, and J. A. Morrison, *J. Am. Chem. Soc.,* **97,** 518 (1975); T. J. Juhlke, R. W. Braun, T. R. Bierschnek, and R. J. Lagow, *ibid.,* **101,** 3229 (1979), have used plasma generated radicals for downstream reactions.

(8) M. Tiecco, *Acc. Chem. Res.,* **13,** 51 (1980).

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