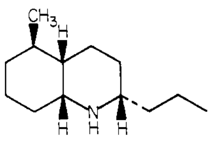
cyclopentylamine formation (entry 1 and 2). More significant is the coupling with aluminum alkynides (entry 11, 19, 22, 23, 24), and synthetically useful propargylic amino derivatives can be prepared in a single operation.

A representative procedure follows: Tri-*n*-propylaluminum (4 mmol, 4 mL of a 1 M hexane solution)[6] was added to a solution of cyclohexanone oxime methanesulfonate (2 mmol, 382 mg) in dry methylene chloride (10 mL) at −78 °C. After 5 min, the solution was warmed to 0 °C and stirred there for 1 h.[7] DIBAH (3 mmol, 3 mL of a 1 M hexane solution) was added at 0 °C, and the reaction mixture was stirred at 0 °C for 1 h. The reaction was terminated by dilution with methylene chloride (~20 mL) followed by successive treatment with sodium fluoride (28 mmol, 1.18 g) and water (21 mmol, 0.38 mL). Vigorous stirring of the resulting suspension was continued at 0 °C for 30 min. Filtration, washing with methylene chloride, and removal of solvent left a pale yellow liquid which was subjected to column chromatography on silica gel (isopropylamine–ether, 1:30) to give 2-propylazacycloheptane (**4**, 180 mg, 64% yield) as a colorless liquid.

The efficiency of our new process is highlighted by the short synthesis of *dl*-pumiliotoxin C (**5**), one of a variety of alkaloids isolated from toxic skin secretions of neotropical frogs *Dendrobates pumilio* and *D. auratur*.[8] The synthesis of the key intermediate **7**[9] for the construction of the desired *cis*-decahydroquinoline is not possible by the obvious route, a direct hydrogenation of the readily available enone **6**,[10] since under the usual hydrogenation conditions, a stereochemical mixture of perhydroindanones was produced. Nonetheless **7** could be prepared in excellent yield from **6** under carefully chosen conditions.[11] Specifically, the selective hydrogenation was realized with reasonable stereoselectivity (~95%)[12] by using palladium black as a catalyst in dioxane in the presence of propionic acid (12 mol %) at 20 °C for 12 h and 1 atm of H_2. Reaction of **7** with hydroxylamine ($NH_2OH{\cdot}HCl$–NaOAc) in methanol at 20 °C for 5 h produced, after one recrystallization from methanol–water, the oxime **8**,[13] mp 101–102 °C, in 84% overall yield from **6**. Treatment of the oxime **8** with *p*-toluenesulfonyl chloride (2 equiv)–pyridine at −20 °C for 1 h and at 0 °C for 5 h followed by trituration with excess cold water produced the oxime tosylate **9**[14] in 90–95% yield. Finally, with tri-*n*-propylaluminum–DIBAH (see Table I), the tosylate **9** was transformed into pumiliotoxin C (**5**) stereospecifically (>99% pure by GC assay) in 60% yield after column chromatography. The spectra of synthetic *dl*-**5** and natural pumiliotoxin C were identical.[15] Using the reaction conditions outlined above, *cis*-decahydroquinoline derivatives can now be prepared in substantial amount without any complex separations.



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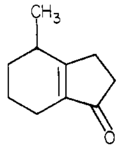

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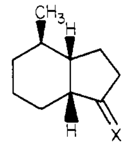

7, X = O
8, X = NOH
9, X = NOTs

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[6] We thank Nippon Aluminum Alkyls, Ltd., for generous gift samples of aluminum reagents.

[7] Any of double alkylation product, 2,2-dipropylazacycloheptane, was not detected from the reaction product. Thus, the alkylation of the resulting imine might be rather slow under these reaction conditions.

[8] Structure: Daly, J. W.; Tokuyama, T. Habemehl, G.; Karle, I. L.; Witkop, B. *Liebigs Ann. Chem.* **1969**, *729*, 198. Daly, J. W.; Witkop, B.; Tokuyama, T.; Nishikawa, T.; Karle, I. L. *Helv. Chim. Acta* **1977**, *60*, 1128. For synthesis (review), see: Inubushi, Y.; Ibuka, T. *Heterocycles* **1977**, *8*, 633 and references cited therein. See also: Overman, L. E.; Jessup, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 5179 and references therein.

[9] Compound **7**: IR (liquid film) 1740, 1462, 1450, 1416, 1380, 1160, 1115, 1061 cm^{-1}.

[10] The enone **6** may be prepared in molar scale from 2-methylcyclohexanone (Stobbe condensation followed by acid treatment). See: El-Abbady, A. M.; El-Ashry, M.; Doss, S. H. *Can. J. Chem.* **1969**, *47*, 1483.

[11] We thank Professor S. Nishimura for helpful discussions for this hydrogenation reaction.

[12] The ratio of $4\beta/4\alpha$ isomer was determined by GC assay (10% Apiezon L on Neopak 1A, 150 °C): t_r of the 4β isomer = 5.46 min; t_r of the 4α isomer = 6.60 min.

[13] ^1H NMR ($CDCl_3$) δ 9.15 (1H, br s, OH), 2.26–2.86 (3 H, m, NCH and NCH_2), 0.94 (3 H, br s, CH_3).

[14] Mp 69–71 °C; ^1H NMR ($CDCl_3$) δ 7.18–8.00 (4 H, m, Ar-H), 2.33–2.90 (3 H, m, NCH and NCH_2), 2.43 (3 H, s, Ar-CH_3), 2.88 (3 H, br s, CH_3).

[15] *dl*-Pumiliotoxin C (**5**) hydrochloride: mp 241–243 °C (lit.[8] 243–244 °C). The ^1H NMR and IR spectra of the synthetic *dl*-**5** hydrochloride were identical in all respects with the reported ones.[8]

Oscillatory Behavior in Fluorescence Intensity from Irradiated Sodium Dodecyl Sulfate Micellar Solutions of Zinc Porphyrin

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Chemical systems maintained far from equilibrium and having a feedback mechanism may show instabilities.[1] The role of light in inducing oscillations, multiple stationary states, and instabilities in chemical systems has been investigated by theoretical and experimental methods. For example, Ross et al. reported that the absorption of light, followed by a radiationless transition, offers the possibility of multiple steady states, damped oscillations, and instabilities,[2] and some investigators reported chaotic or periodic oscillations induced by light.[3] We wish to report our observation concerning unusual variation of fluorescence intensity of zinc protoporphyrin dimethyl ester in a sodium dodecyl sulfate (SDS) micellar system. Excitation of the fluorescence of zinc protoporphyrin in SDS micelles at 410 nm results in behavior giving rise to chaotic oscillations in emission intensity at 580 nm. Findings of this kind were reported for the chemical system dissolved in an organic solvent, which displayed temporal or spatial oscillations.[3,5] We consider it important to report the observation of fluctuations in fluorescence of zinc protoporphyrin in a micellar system, in contrast with the case of organic solutions.

The work was prompted by the desire to carry out fluorescence quenching experiments on zinc protoporphyrin in micelles. We found that excitation of an SDS solution of zinc protoporphyrin produces fluorescence which varies in time after an induction period and this variation of intensity disappears when organic quenchers are added to the micellar solutions.

Zinc protoporphyrin dimethyl ester was prepared from protohemin[4] and purified by silica gel column chromatography; the purity of this substance was confirmed by silica gel TLC and reversed-phase HPLC with an octadecylsilane-treated silica gel column. The SDS employed in this experiment was purified by Soxhlet extraction with hexane and recrystallization from water–acetone. The observation was made with a Hitachi MPF-2A fluorescence spectrometer which was equipped with a Haake D3 temperature-regulated cell holder, and the fluorescence spectra were normally recorded at 298 K. Zinc protoporphyrin was dissolved in only a small amount of methanol, and this methanol solution was added dropwise into a large amount of SDS solution. The sample cell was stoppered but not degassed.

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[1] G. Nicolis and I. Prigogine, "Self-Organization in Nonequilibrium Systems", Wiley, New York, 1977.

[2] A. Nitzan and J. Ross, *J. Chem. Phys.*, **59**, 241 (1973).

[3] T. L. Nemzek and J. E. Guillet, *J. Am. Chem. Soc.*, **98**, 1032, (1976). I. Yamazaki, M. Fujita, and H. Baba, *Photochem. Photobiol.*, **23**, 69 (1976). R. W. Bigelow, *J. Phys. Chem.*, **81**, 88 (1977). M. D. Donne and P. Ortoleva, *ibid.*, **67**, 1861 (1977).

[4] K. Smith, Ed., "Porphyrins and Metalloporphyrins", Elsevier, Amsterdam, 1975.

[5] R. J. Bose, J. Ross, and M. S. Wrighton, *J. Am. Chem. Soc.*, **99**, 6119 (1977).

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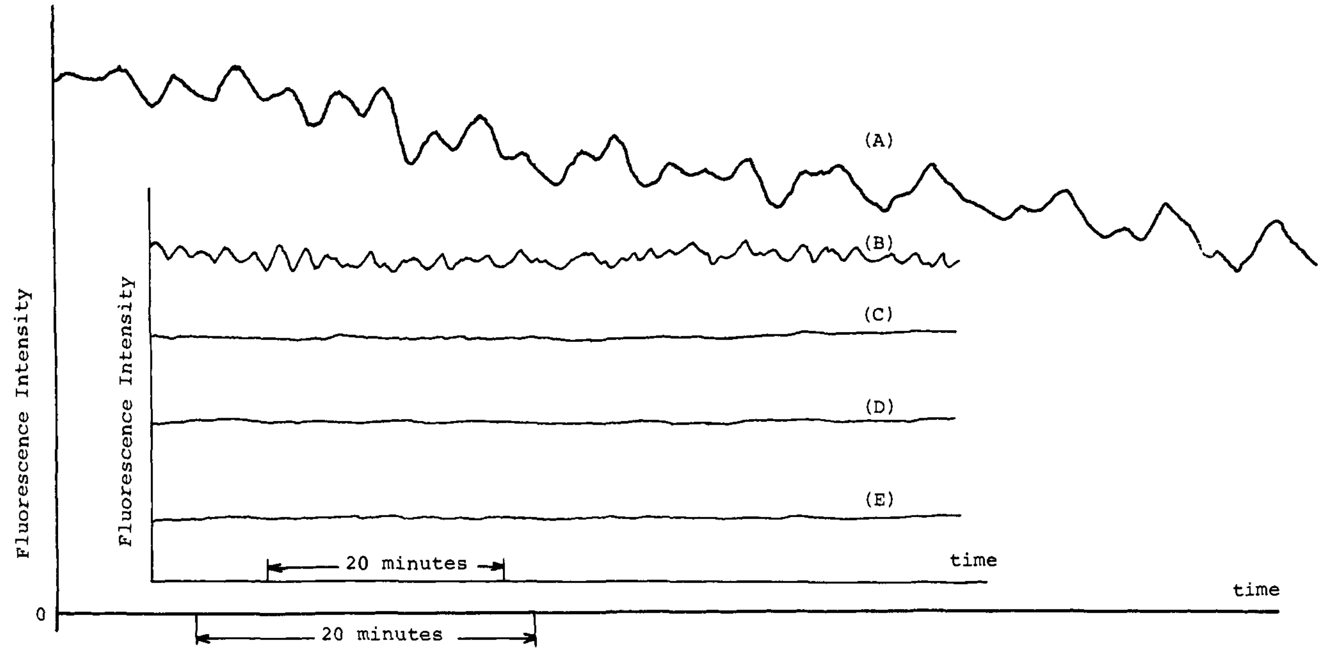

Figure 1. Plots of fluorescence intensity against time at 298 K. (A) Zinc protoporphyrin dimethyl ester in 0.05 M SDS solution. The base line is shown for this line (number 0). (B) Zinc protoporphyrin dimethyl ester in 0.08 M SDS solution. (C) Zinc protoporphyrin dimethyl ester in MeOH. (D) Zinc protophryin dimethyl ester in HTAB solution. (E) Ruthenium tris(bipyridyl) in SDS solution. All curves of zinc protoporphyrin dimethyl ester are for an excitation wavelength of 410 nm and an emission wavelength of 580 nm.

The measurements of fluorescence intensity were performed at several times over a period of 2 weeks because some aging of the micellar solution is necessary to obtain reliable results. Chaotic variations in fluorescence intensity were observed during these experiments, and the overall intensity of absorption in the visible spectrum declined steadily with time. Figure 1 shows typical plots of zinc protoporphyrin fluorescence intensity at 580 nm against time in ~3 mL of SDS micellar solution at 298 K. As the Soret band of zinc protoporphyrin in SDS micelles was observed at 412 nm, the fluorescence was excited at 410 nm during these measurements. Under the usual conditions, chaotic oscillations as shown in Figure 1 were observed. Figure 1 also contains the results in methanol and in hexadecyltrimethylammonium bromide (HTAB) micelles. The variation in fluorescence intensity in the methanol solution was not observed, as shown in Figure 1. In the case of HTAB micelles, the variation was also not observed under the same conditions as those of SDS, but a slight variation was observed when the sample cell was irradiated by a higher intensity of light or the concentration of HTAB was greatly increased. The fluorescence intensity of tris(bipyridyl)ruthenium complex in an SDS micellar system was measured to check the properties of the micellar system employed in this experiment, and no fluctuations were observed in the emission spectrum. In addition, measurements of anthracene in methanol also gave the same results. Thus, the observation about zinc protoporphyrin is real and independent of the source of the instrumentation and of the chemical materials, such as impurity.

In the measurements on the SDS micelles, the overall fluorescence intensity gradually declined and the amplitude of variation increased with time. The rate of decrease increases with an increase in light intensity. However, the period and the pattern of the variation in intensity of fluorescence and the induction time were not always reproducible. When the solution was stirred, the chaotic variation ceased and the intensity increased instantly and then showed a gradual steady decline. However, the variation in intensity commenced again when the stirring was stopped and the solution was quiet. This result may indicate that the variation is dependent on localizations rather than on overall bulk concentrations. This behavior is similar to that of other systems reported already.[3,5] In addition, when a quencher (methylviologen) was added to the SDS solutions, the fluctuations ceased and the overall intensity in fluorescence decreased. The intensity of the Soret band of zinc protoporphyrin in the SDS micellar system is decreased by the irradiation of light for a long time, indicating decomposition of the porphyrin skelton. Though we do not have a detailed interpretation of this observation, the experimental results appear interesting and directly related to the occurrence of chemical instabilities. A detailed analysis of many features of this phenomenon is in progress.

P-450-Type Dioxygen Activation Using H_2/Colloidal Pt as an Effective Electron Donor

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The catalytic cycle of cytochrome P-450, an important heme-containing monooxygenase of liver microsomes, involves the NADH-dependent *reductive dioxygen activation* to give an active oxidizing species having a Fe–O bond.[1] This unique oxidizing species has absorbed increasing attention of chemists. Successful oxygen atom transfer from iodosylbenzene to synthetic iron(III) porphyrins,[2] P-450, or other metal ion porphyrins[3,4] were reported. The reductive dioxygen activation was first modeled by us using a totally artificial system, $NaBH_4$–(tetraphenylporphinato)man-

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(1) (a) Sato, R.; Omura, T. In "Cytochrome P-450": Kodansha Ltd.: Tokyo, 1978. (b) Boyd, G. S.; Ullrich, V. *Biochem. Soc. Trans.* **1975**, 803. (c) Nordblom, G. D.; White, R. E.; Coon, M. J. *Arch. Biochem. Biophys.* **1976**, *175*, 524. (d) Hrycay, E. G.; Gustafsson, J.; Ingelman-Sundberg, M.; Eruster, L. *Biochem. Biophys. Res. Commun.* **1975**, *66*, 209.

(2) (a) Presented by Groves, J. T. at the American Chemical Society/Chemical Society of Japan Chemical Congress, Honolulu, April 1979. (b) Groves, J. T.; Nemo, T. E.; Myers, R. S. *J. Am. Chem. Soc.* **1979**, *101*, 1032. (c) Chang, C. K.; Kuo, M.-S. *J. Am. Chem. Soc.* **1979**, *101*, 3414. (d) Groves, J. T.; Krichnan, S.; Avaria, G. E.; Nemo, T. E. "Biomimetic Chemistry"; American Chemical Society: Washington, DC, 1980; Adv. Chem. Ser. No. 191.

(3) Groves, J. T.; Kruper, W. J., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 7613.

(4) (a) Hill, C. L.; Schardt, B. C. *J. Am. Chem. Soc.* **1980**, *102*, 6374. (b) Groves, J. T.; Kruper, W. J., Jr.; Hanshalter, R. C. *Ibid.* **1980**, *102*, 6375.

0002-7863/81/1503-7371$01.25/0