rate substantially greater than the rate of rotation about the α,β-carbon–carbon single bond.

In accord with this mechanism, the rate of attack by hydride (*cf.* Table I) is facilitated by α-alkyl groups as these will stabilize the radical III. β Substituents retard the reaction presumably by sterically hindering the approach of the hydride.[8]

[8] The authors express their thanks to the referees for helpful comments and for drawing their attention to ref 1j.

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Cyclodimerization of Styrene[1]

Sir:

The dimerization of styrene occurs thermally,[2] photochemically,[2] and by ionic mechanisms, either cationic[3] or anionic,[4] with characteristic product patterns. It is thus of potential mechanistic significance to identify dimeric radiolysis products of styrene. The benzene-sensitized radiolysis, if actuated by triplet benzene as in *cis–trans* isomerizations of olefins,[5] should correlate with the photosensitized dimerization. In this communication it is shown that the correlation has limited validity. The argument rests mainly on the previously uncharacterized stereochemistry of diphenylcyclobutane formation in variously initiated dimerizations.

The new measurements (Table I) were made at low conversions (0.1–0.5% dimer) to minimize subsequent isomerization of the radiation-sensitive and thermally labile diphenylcyclobutanes. In dilute solutions at these conversions, high polymer formation was not qualitatively noticeable or detectable by analysis for unreacted monomer. The C_{16} fractions were analyzed, with bibenzyl as internal standard, by chromatography on lightly loaded QF-1 columns at 135°. γ Irradiations were performed at a dose rate of 4×10^{17} eV/g min with total doses of 4×10^{19} to 4×10^{20} eV/g. Ultraviolet irradiations utilized a high-pressure mercury lamp and appropriate filters with solutions in sealed Pyrex cells at 30°. Yields of *cis*- and *trans*-1,2-diphenylcyclobutanes (**1** and **2**, respectively) were satisfactorily reproducible but the relative yields of 1-phenyltetralin (**3**) and 1-phenyl-1,2-dihydronaphthalene (**4**) in the thermal and radiolytic reactions were somewhat erratic despite care to exclude air. Addition of *t*-butylcatechol, considered as a possible antioxidant, actually increased the yield of **4** and decreased **3**. The yield of 1-phenylnaphthalene was appreciable in direct photolysis (7% of total dimer) but small in other cases and unobserved in sensitized photolysis. In radiolysis, two unidentified components, eluting between **1** and **3**, contributed together less than 10%.

Table I. Composition of Styrene Dimer Fractions[a]

Conditions	1	2	3	4
A. Radiolysis[b]				
0.04 *M* styrene in benzene	3.1	1.1	5.3	1.1
0.2 *M*, 0.1% *t*-BC,[c] in benzene	7.4	3.7	11.1	11.0
0.2 *M*, 1 atm N_2O, in benzene	7.2	3.3	6.2	6.6
Neat, with 0.1% *t*-BC	22.8	25.9	4.1	11.2
B. Sensitized Photolysis[d]				
Sensitizer[e] 0.01–0.02 *M*	0.22	0.75	0.03	. . .
C. Direct Photolysis[f]				
Benzene	0.75	0.10	0.08	. . .
Methylene chloride	0.72	0.14	0.07	. . .
D. Thermal[g]				
No additive	0.09	0.21	0.59	0.02
0.1% *t*-BC	0.18	0.36	0.11	0.29

[a] Products: **1**, *cis*-1,2-diphenylcyclobutane; **2**, *trans*-1,2-diphenylcyclobutane; **3**, 1-phenyltetralin; **4**, 1-phenyl-1,2-dihydronaphthalene; composition given as mole fraction, except in radiolysis. [b] Cobalt-60 γ irradiation at 25°; yields as *g* values × 100. [c] *t*-Butylcatechol. [d] Photosensitized (uranium glass filter); 0.2 *M* styrene in benzene. [e] Averaged results for benzophenone, xanthenone, phenyl cyclopropyl ketone, and anthraquinone. [f] Direct photochemical, 0.8 *M* styrene, various solvents. Similar results were found in methanol, diethyl ether, and isohexane at 30° or at −80°. [g] Thermal, 0.2 *M* styrene in benzene, 110°, 120 hr.

Dimer yields in the radiolysis of dilute solutions are low compared with *g* values for benzene triplet production of 5 and higher from *cis–trans* isomerizations,[6] and even in neat styrene the total dimer represents a *g* of less than 1. The dimerization in dilute solution is more than the fractional energy absorbed by monomer would account for and can thus be described as benzene sensitized. Cationic mechanisms are evidently not involved, since the characteristic open-chain olefins and indan derivatives are absent, but an anionic, or solvated electron, mechanism is admissible for at least part of the observed 1-phenyltetralin.[7]

The products of primary interest are **1** and **2** since they are the main products in sensitized photolysis and presumably arise by an excited-state mechanism. There is disagreement in the isomer yields; *cis* predominates in radiolysis by a factor of 2 whereas photolysis, with any of the sensitizers tried, favors *trans* by a factor of 3.4. In direct photolysis, with singlet excitation by absorption in the long-wavelength band of styrene, the situation is again reversed, *cis* being favored under widely different conditions by a factor of ~6. This is evidently an example, not the first,[8] of dimerization through strong *cis*-pairwise complexing of the excited singlet. A *cis*/*trans* ratio in radiolysis that is midway between the two photochemical situations is the basis for concluding that cyclobutane formation in the radiolysis of benzene solutions occurs about equally by triplet and singlet excitation.

The thermal formation of diphenylcyclobutanes, not allowed[9] as a one-step process, may be related to photosensitized dimerizations through a common inter-

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[1] Work performed under the auspices of the U. S. Atomic Energy Commission.

[2] F. R. Mayo, *J. Am. Chem. Soc.*, 90, 1289 (1968).

[3] B. B. Carson, J. Dorsky, J. E. Nickel, W. M. Kutz, and H. I. Thayer, *J. Org. Chem.*, **19**, 17 (1954).

[4] A. Zwierzak and H. Pines, *ibid.*, **28**, 3392 (1963).

[5] E. Fischer, H. P. Lehmann, and G. Stein, *J. Chem. Phys.*, **45**, 3905 (1966), and earlier literature therein cited.

[6] M. A. Golub and C. L. Stephens, *J. Phys. Chem.*, 70, 3576 (1966).

[7] The supposedly anionic dimerization, in refluxing styrene with potassium *t*-butoxide, to 1-phenyltetralin only[4] was under conditions that would allow thermal dimerization and isomerization of primary products.

[8] D. O. Cowan and R. L. Drisko, *J. Am. Chem. Soc.*, **89**, 3068 (1967).

[9] R. Hofmann and R. B. Woodward, *ibid.*, **87**, 2046 (1965).

mediate, possibly the Flory[10] diradical. If so, the stereochemical pattern should be the same; presently available data, not strictly comparable as to temperatures, show order-of-magnitude agreement with a thermal *trans/cis* ratio of 2.2 compared with 3.4 in sensitized photolysis. A further mechanistic correlation accommodates by-products in the 1-phenyltetralin series in photolysis and radiolysis since a 1,6 closure would form the Diels–Alder dimer that, in Mayo's[2] thermal mechanism, is the required precursor. Conversely, in the thermal reaction, this dimer is a possible precursor also in cyclobutane formation since, on bond energy considerations, it is intermediate between styrene and diradical. The still hypothetical Diels–Alder dimer is doubtless a sensitive substance but conceivably could be made in demonstrable amount by low temperature sensitized photolysis of styrene.

Although the radiolysis experiments here described have revealed no products of unequivocally ionic origin, further experimentation should be performed under conditions of intensive drying since, in high polymer formation, this condition is now known[11] to favor ionic mechanisms.

(10) P. J. Flory, *J. Am. Chem. Soc.*, **59**, 241 (1937).

(11) F. W. Burns, R. M. O'Connor, and D. C. Pepper, *J. Polym. Sci., Part B*, **5**, 1059 (1967), and earlier cited literature.

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The Structure of Batrachotoxinin A, a Novel Steroidal Alkaloid from the Colombian Arrow Poison Frog, *Phyllobates aurotaenia*

Sir:

Earlier studies[1,2] on the potent venom from the Columbian arrow poison frog[3] had indicated the presence of three major alkaloids, batrachotoxin, batrachotoxinin A, and batrachotoxinin B. Batrachotoxin, the most active cardiotoxin known (ED_{50}, intravenous in anesthetized dogs,[4] $<0.5\ \mu g/kg$), was the major steroid alkaloid isolated from these frogs.

When the earlier isolation (distribution between two solvents, preparative tlc) procedures[1,2] were modified and all operations carried out at 5°,[5] very little batrachotoxinin A was present after the initial purification. The major active fraction has now been resolved into two very similar isomers of almost equal toxicity, *viz.*, batrachotoxin (LD_{50}, subcutaneous in mice, 2 μg/kg) and isobatrachotoxin (LD_{50}, 3 μg/kg). In addition, a third component, pseudobatrachotoxin, is present in the extracts and cochromatographs with isobatrachotoxin. It is very unstable and readily converted to batrachotoxinin A, formally by the addition of the elements of water. Thus, batrachotoxinin A is probably a secondary product formed from the highly unstable pseudobatrachotoxin during purification. Batrachotoxinin A (LD_{50}, 1 mg/kg), which retains only $^{1}/_{600}$ of the toxicity of the original venom, is still almost as toxic as strychnine (LD_{50}, 0.5 mg/kg).[6]

Pure batrachotoxin, isobatrachotoxin, and batrachotoxinin A have now been isolated by column chromatography on silica gel (20W) and by elution with a mixture of cyclohexane, chloroform, triethylamine, and methanol (16:4:1:1). If one assumes that all the batrachotoxinin A arises from pseudobatrachotoxin, then batrachotoxin, isobatrachotoxin, and the sum of pseudobatrachotoxin and batrachotoxinin A occur in fresh extracts in the ratio of 3:1:5. The fragmentation pattern of the high-resolution mass spectrum (AEI MS-9 mass spectrometer, direct inlet 240°) indicates the close relationship of the three isomers ($C_{24}H_{33}NO_4$). Infrared spectra of batrachotoxin[1,2] and isobatrachotoxin show an intense absorption band at 1690 cm^{-1} which is missing in batrachotoxinin A. The band previously reported[2] at 1645 cm^{-1} for batrachotoxinin A is due to an impurity. The ultraviolet spectra of batrachotoxin and isobatrachotoxin are virtually identical and have characteristic maxima at 234 mμ (ϵ 9200) and 264 mμ (ϵ 5100). Batrachotoxinin A and pseudobatrachotoxin have only end absorption as judged from direct measurement and from difference spectra of isobatrachotoxin compared with mixtures of pseudobatrachotoxin and isobatrachotoxin. The previous assumption of only end absorption for batrachotoxin[1,2] rested on the low extinction coefficients now considered to be caused by the presence of pseudobatrachotoxin.

Batrachotoxinin A ($C_{24}H_{35}NO_5$) has now been acylated with *p*-bromobenzoic anhydride under Schotten–Baumann conditions to an O-*p*-bromobenzoate. This product was purified by column chromatography on silica gel (10W) with chloroform containing 3% methanol and recrystallized from acetone to yield fine needles (mp 213°). Mass spectrometry established the composition as $C_{31}H_{38}NO_6Br$. Saponification of this *p*-bromobenzoate with 0.05 *N* alkali at room temperature gave back batrachotoxinin A and not a new or rearranged product.

An X-ray diffraction analysis of a single crystal of this derivative was made using three-dimensional intensity data which were collected using Cu Kα radiation and the equiinclination, multiple-film Weissenberg technique. It was possible to record only a total of 830 independent reflections from a crystal 0.05 × 0.03 mm in cross section. The material crystallizes in the orthorhombic system, space group $P2_12_12_1$ with four molecules in the unit cell and cell dimensions $a = 15.42 \pm 0.03$ Å, $b = 7.05 \pm 0.02$ Å, and $c = 26.50 \pm 0.04$ Å. The Br atom was readily located from a Patterson map to be at 1/5,0,0 and phases based on the position of the Br atom alone gave rise to an electron density map with a fourfold ambiguity for the remainder of the structure. It was possible to identify the two oxygen atoms for the *p*-bromobenzoate group in this map, and thus locate approximately the *p*-bromobenzoate group in the unit cell. Using this group as a known partial structure, phases were obtained for some of the strongest reflections. These phases were used with the tangent formula in recycling procedure[7] to

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(1) F. Märki and B. Witkop, *Experientia*, **19**, 239 (1963).

(2) J. W. Daly, B. Witkop, P. Bommer, and K. Biemann, *J. Am. Chem. Soc.*, **87**, 124 (1965).

(3) Previously referred to as *Phyllobates bicolor;* see footnote 22 in J. W. Daly and C. W. Myers, *Science*, **156**, 970 (1967).

(4) L. S. Harris and F. J. Rosenberg, personal communication. This dose causes interference with conduction in the heart and produces extra systoles. Slightly higher doses cause ventricular fibrillation and death. Little effect on blood pressure was noted.

(5) J. W. Daly and B. Witkop, *Mem. Inst. Butantan, Suppl. Comemorative*, **2**, in press.

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(7) J. Karle, *Acta Cryst.*, **21**, in press.