Photochemically Generated Benzyne[1]

MAITLAND JONES, JR.,* AND MARK R. DECAMP[2]

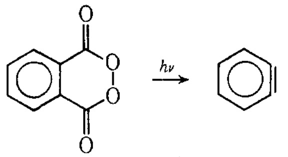
Department of Chemistry, Princeton University, Princeton, New Jersey 08540

Received November 6, 1970

Photolysis of phthaloyl peroxide through Pyrex yields benzyne. The intermediate generated undergoes a stereospecific 2 + 4 and nonstereospecific 2 + 2 cycloaddition and is thus identical in symmetry properties with that formed by conventional decomposition of benzenediazonium-2-carboxylate. Reaction with low-boiling compounds is facilitated by this method and higher yields of products often are obtained. Benzyne reacts with methylacetylene, allene, and cyclopropane in ene fashion to give phenylallene, benzylacetylene, and allylbenzene, respectively.

Remarkable indeed is the relative absence from the chemical literature of references to the photochemical generation of benzyne. Flash photolysis of benzenediazonium-2-carboxylate by Berry and coworkers has been reported[3-6] and a variety of precursors has been briefly mentioned in Hoffmann's book.[7] It is notable, however, that only two-three pages are required for a description of the "Generation of Dehydrobenzene by Photolytic Methods." [7] Of the 155 Diels-Alder reactions tabulated in ref 7, only three involve photochemically generated benzyne.

We were drawn to find a photochemical source of benzyne for several reasons. First, we hoped to detect reactions of either the excited singlet or triplet state and, second, it seemed to us that a photochemical method of generating benzyne would facilitate the investigation of reactions with low-boiling hydrocarbons. We hoped both to achieve better yields in the few reactions that had been done and to find new reactions.



Here we amplify earlier reports[8,9] on the photolysis of phthaloyl peroxide. (*Caution*—see Experimental Section.) The main difficulty in this reaction is the insolubility of phthaloyl peroxide in most hydrocarbon solvents. Wittig and Ebel[9] used benzene as solvent but were able to isolate only a 7.4% yield of Diels-Alder adduct from tetracyclone. We find that the use of acetone or tetrahydrofuran allows formation of homogeneous solutions of phthaloyl peroxide in hydrocarbons. Using this modification of the earlier procedure,[9] reasonable yields can usually be achieved.

Stereochemical Studies.—We chose first to examine the 2 + 2 cycloaddition reaction. For the same reasons given earlier[10] (largely lack of ene reaction), the substrate used was *cis*- or *trans*-1,2-dichloroethylene. Irradiation, followed by analytical and preparative gas-liquid partition chromatography (glpc) on a 2-m, 10% DC-710 silicone oil column gave, in addition to dimers, oligomers, and polymers of the dichloroethylenes, *cis*- and *trans*-1,2-dichlorobenzocyclobutene in 18-35% yield, depending upon the concentration of olefin and length of irradiation (Table I). After some hours of irradiation, glpc analysis revealed that, even though phthaloyl peroxide remained, the only reaction taking place was dimerization of the dichloroethylene.

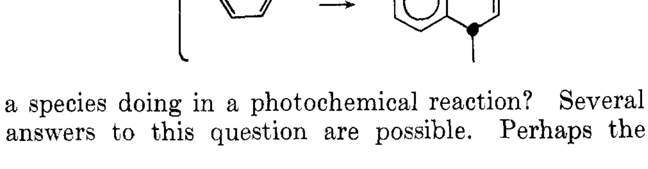
TABLE I

STEREOCHEMISTRY OF THE 2 + 2 CYCLOADDITION OF BENZYNE

Mode[a]	Olefin	% cis adduct	% trans adduct
Δ	trans	19	81
Δ	cis	68	32
hν	trans	17[b]	83
hν	cis	69[b]	31

[a] Thermal source was benzenediazonium-2-carboxylate hydrochloride.[10] [b] Independent of choice of acetone or tetrahydrofuran as solvent.

The stereochemistry of the 2 + 4 reaction was also tested, and here too agreement with earlier work[10] was found. Irradiation of phthaloyl peroxide in *trans,-trans*-hexadiene-2,4 gave, as nearly as we can tell, the single dimethyldihydronaphthalene previously identified as cis.[10] The cis and trans isomers do not separate on glpc, but time-average scans of the vinyl region of the nmr spectrum allow the detection of very small amounts of the trans isomer. Under conditions where 2% of the trans material would be detected with ease, we see none. The combination of a nonstereospecific (and therefore very probably nonconcerted) 2 + 2 reaction with a stereospecific (and thus probably concerted) 4 + 2 reaction makes the intermediacy of the same, symmetric singlet state found in the thermal reaction highly probable. The question is, what is such a species doing in a photochemical reaction? Several answers to this question are possible. Perhaps the



---

(1) Support of this work by the National Science Foundation is gratefully acknowledged (Grant GP-12759).

(2) University Fellow, 1969-1970.

(3) R. S. Berry, G. N. Spokes, and R. M. Stiles, *J. Amer. Chem. Soc.*, **82**, 5240 (1960).

(4) R. S. Berry, G. N. Spokes, and M. Stiles, *ibid.*, **84**, 3570 (1962).

(5) R. S. Berry, J. Clardy, and M. E. Schafer, *ibid.*, **86**, 2738 (1964).

(6) M. E. Schafer and R. S. Berry, *ibid.*, **87**, 4497 (1965).

(7) R. W. Hoffmann, "Dehydrobenzene and Cycloalkynes," Academic Press, New York, N. Y., 1967.

(8) L. Horner and H. Brüggemann, *Ann.*, **635**, 22 (1960).

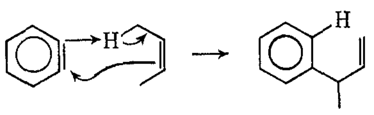
(9) G. Wittig and H. F. Ebel, *ibid.*, **650**, 20 (1961).

(10) M. Jones, Jr., and R. H. Levin, *J. Amer. Chem. Soc.*, **91**, 6411 (1969).

reactions of S^1 and S^0 benzyne are the same, or we are gaining entry to S^0 directly or through internal conversion from S^1. The first of these possibilities appears unlikely to us, as the control of orbital symmetry over the stereochemical details of reactions seems sufficiently well established[11] to warrant confidence in the proposition that the excited and ground states will differ in their addition reactions. We have not observed an excited state of benzyne.

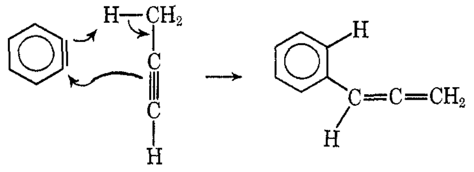
Other Known Reactions.—In this section we would like to demonstrate the utility of the photolytic reaction. When phthaloyl peroxide rather than a more conventional benzyne precursor is used, higher yields of products often can be obtained. Sometimes the increased yields allow the isolation of new products. For instance, butadiene was found to give a Diels–Alder adduct in 10% yield.[12] A later article reported 9%,[13,13a] and some years ago traces were probably obtained through photolysis of benzenediazonium-2-carboxylate.[3] Photolysis of phthaloyl peroxide in butadiene gives a 20% yield[14] of two products in the ratio of 4:1. We isolate, in addition to the Diels–Alder adduct, the product of the 2 + 2 cycloaddition. 1,4-Dihydronaphthalene is known[12] but 1-vinylbenzocyclobutene was not. Mass spectral analysis confirmed the elemental composition as $C_{10}H_{10}$, and examination of the nmr and uv spectra left no doubt as to the detailed structure. The crucial features of the nmr spectrum are the signals for the vinyl group at τ 3.70–4.25 (1 H) and 4.68–5.17 (2 H), a doubly allylic proton at 5.80–6.17 (1 H), and a multilined pattern at 6.45–7.35 (2 H). The uv spectrum [$\lambda_{\max}^{\text{cyclohexane}}$ 272, 266, 261, 253 (sh) nm] is most similar to that of the vinylbenzocyclobutene isolated by Wittig and Dürr[12] from the 2 + 2 cycloaddition of benzyne and 2,3-dimethylbutadiene (272, 266, 260 nm).

The ene reaction[15] is very common in benzyne chemistry and we have discovered several, including some new types, on photolysis of phthaloyl peroxide. *cis*-Butene-2 gives a single major product, 3-phenylbutene-1 in *ca.* 9% yield.[14] The yield is not spectacularly high but should be compared with 4% reported for reaction with isobutylene[12] and 13% for 2,3-dimethylbutene-2.[16] Similarly, propylene gives *ca.* 10% of the ene product, allylbenzene.

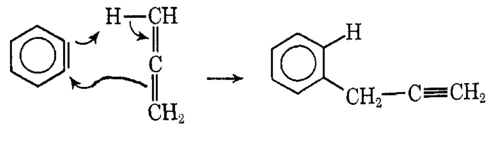


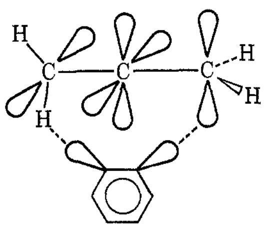
Previously Unknown Reactions.—While all of the examples mentioned above are known, many (but not all) are significantly easier to run using the photochemical method than the thermal. In this section we describe some new reactions with low-boiling hydrocarbons. We suspect that they have not previously been reported at least partially because of the inconvenience of the usual thermal sources of benzyne.

Perhaps our first example, the reaction with methylacetylene, does not really qualify as new, since a similar reaction is mentioned in Hoffmann's book.[17] No details have appeared, however, and our yield is substantially greater. We find a 16% yield[14] of phenylallene on irradiation of phthaloyl peroxide in methylacetylene Identification was by comparison with an authentic sample, and the mechanism of formation presumably involves an ene reaction.

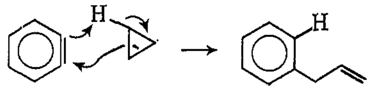


A different kind of ene reaction appears in the reaction with allene. Again a single major product, benzylacetylene, is formed in 15% yield.[14] An ene reaction is implicated, but it is not of the usual sort. The orbitals involved are well aligned for such a reaction, although proof of concertedness is lacking. No evidence could be found for the product of a 2 + 2 cycloaddition, although Wasserman and Fernandez[18] have postulated such a process in the reaction of benzyne with phenylethoxyallene, generated *in situ* from 1-ethoxypropyne and benzyne.[18a]





Although a number of reactions with single bonds of strained hydrocarbons have been reported,[19–21] the parent of these, the reaction with cyclopropane, has escaped detection. We find that benzyne adds in ene fashion to cyclopropane to give, along with a large amount of polymer, 3–4% of allylbenzene. Indan was specifically sought and not found.



---

[11] R. Hoffmann and R. B. Woodward, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970.

[12] G. Wittig and H. Dürr, *Ann.*, **672**, 55 (1964).

[13] L. F. Hatch and D. Peter, *Chem. Commun.*, 1499 (1968).

[13a] Note Added in Proof.—See, however, footnote † in R. W. Atkin and C. W. Rees, *Chem. Commun.*, 152 (1969).

[14] Our yields do not generally reflect the fact that peroxide remains at the end of our reaction times. In a typical case, 20% of the peroxide was found remaining; a general upward correction by a factor of 1.25 is perhaps warranted.

[15] For a review of the ene reaction, see H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 556 (1969).

[16] G. Wittig and R. W. Hoffmann, *Chem. Ber.*, **95**, 2718 (1962).

[17] A private communication from M. Stiles and A. Haag (ref 7, p 198) reports a <4% yield of phenyl-*n*-propylallene from benzyne and hexyne-1).

[18] H. H. Wasserman and J. M. Fernandez, *J. Amer. Chem. Soc.*, **90**, 5322 (1968).

[18a] Note Added in Proof.—While this article was in press a communication on the reaction of benzyne with allenes appeared: H. H. Wasserman and L. S. Keller, *Chem. Commun.*, 1483 (1970).

[19] M. Pomerantz, G. W. Gruber, and R. N. Wilke, *J. Amer. Chem. Soc.*, **90**, 5040 (1968).

[20] P. G. Gassman and G. D. Richmond, *ibid.*, **90**, 5637 (1968).

[21] P. G. Gassman and G. D. Richmond, *ibid.*, **92**, 2090 (1970).

In summary, photolysis of phthaloyl peroxide yields a benzyne with the same symmetry properties as those generated in more conventional ways.[10] Reactions with low-boiling hydrocarbons are easy to run and often give higher yields than those of thermally generated benzyne. New reactions of benzyne with methylacetylene, allene, and cyclopropane are described. We hope in the future to report on their mechanisms.

Experimental Section

General.—Nuclear magnetic resonance spectra were recorded at 60 MHz on a Varian A-60A spectrometer. Nmr data of all products trapped from the vpc were obtained in capillary tubes with CCl_4 as solvent and tetramethylsilane added as an internal standard. Samples are collected directly from the gas chromatograph in Pyrex tubes slightly smaller than an ordinary melting point capillary. Solvent is added and the sealed tube mounted in a sawed-off nmr tube. Mounting techniques vary, but a current favorite involves wrapping the capillary in Scotch tape until it just fits the nmr tube. We heartily recommend the microtube technique as it allows analysis of samples as small as 1 mg. Mass spectra were measured on an AEI MS-9 mass spectrometer.[22] Uv spectra were run on a Cary 14 recording spectrophotometer. Gas chromatographic analyses and collections were performed on an Aerograph A90P chromatograph with the following columns: (A) 2 m, 10% DC-710 on 60–80 mesh Chromosorb W; (B) 1 m, 10% DC-550 on 60–80 mesh Chromosorb P. Yields were determined gas chromatographically and were not corrected for thermal conductivities. All photolyses were carried out with a Hanovia 450-W medium-pressure mercury arc shielded with Pyrex filters.

Phthaloyl Peroxide.—(*Caution*—see below.) Phthaloyl peroxide (PPO) was prepared in 40% yield by a slight modification of the method of Russell.[23] To an ice-chilled solution of 16 g each of K_2HPO_4 and KH_2PO_4 in 400 ml of water was added 8.3 g (0.11 *M*) of Na_2O_2. This solution was stirred vigorously in an ice bath during the addition of a chilled solution of 20.3 g (0.1 *M*) of *o*-phthaloyl dichloride in 300 ml of chloroform. The two-phase system was stirred for 15 min in an ice bath. The layers were separated and the organic portion dried over $MgSO_4$ and evaporated to dryness at the water pump. The white solid which remained was collected and washed repeatedly with hexane. After drying *in vacuo* overnight, the yield of white powder [mp 124.5–125° dec (lit.[23] 126°)] was 6–7 g. The product was *not* recrystallized and was stored in the freezer until use.

Warning. Upon melting a small sample of the peroxide in a capillary tube, there was a sharp, explosive report at 123°. PPO could also be detonated by striking with a hammer or by ignition. We experienced no trouble with phthaloyl peroxide during ordinary laboratory operations, but as with any peroxide it should be handled with utmost respect.

Photolysis of PPO in *trans*-Dichloroethylene (TDCE) and *cis*-Dichloroethylene.—PPO (300 mg) was dissolved in 5 ml of acetone and a large excess (*ca.* 10 ml) of TDCE. Irradiation in a Pyrex tube for 5 hr provided two products in the ratio 1:5 in addition to a number of olefinic photoproducts. The course of the photolysis was monitored by gas chromatography on column A at 150°. After *ca.* 3 hr the increase in cycloaddition products was negligible, although unreacted peroxide remained; *cis*- and *trans*-dichlorobenzocyclobutene were isolated by preparative gas chromatograph on column A with retention times of 16.5 and 7 min, respectively. They were identified by comparison with authentic samples. The overall yield of cycloaddition products ranged from 18 to 35% as determined by gas chromatography through addition of biphenylene as an internal standard.

The irradiation of PPO was also performed in *cis*-dichloroethylene (CDCE). PPO (320 mg) was dissolved in 10 ml of CDCE and 5 ml of acetone and irradiated for 6 hr in a Pyrex tube. Monitoring the progress of the reaction by gas chromatography indicated the rate of cycloaddition was very slow relative to the reaction in the trans olefin. The two cycloaddition products were obtained in a 7:3 ratio in very low yield.

Photolysis of *trans*-Dichlorobenzocyclobutene.—A sample of this material in TCDE was irradiated for 2 hr in an nmr tube and no isomerization could be observed.

Photolysis of PPO in *trans,trans*-Hexadiene-2,4.—PPO (300 mg) was dissolved in 5 ml of acetone and a 20-fold excess of *trans,trans*-hexadiene-2,4 (Chem Samples Co.) and sealed under nitrogen in a Pyrex tube. The solution was irradiated for 6.5 hr, after which it was concentrated and injected into the gas chromatograph (column B). In addition to a multitude of higher boiling products (retention times up to 30 min at 180°), *cis*-1,4-dimethyl-1,4-dihydronaphthalene was isolated by preparative gas chromatography (retention time 4.5 min at 130°) and identified by comparison with a known sample. The vinyl region of the spectrum was swept 60 times with a Varian Associates C-1024 Computer of Average Transients. No *trans*-1,4-dimethyl-1,4-dihydronaphthalene could be detected by the peak due to its vinyl protons, which appear *ca.* 15 Hz upfield from the peak for the vinyl hydrogens of the cis compound. Two per cent could easily have been seen under these conditions. This analytical method was made necessary because the two isomers were inseparable by gas chromatography in our hands.

Photolysis of PPO in *cis*-Butene.—Into a solution of 292 mg of PPO in 5 ml of acetone in a thick-walled Pyrex tube cooled to −78° was condensed 15 ml of *cis*-butene. The tube was carefully sealed under nitrogen and irradiated at room temperature for 10 hr. After irradiation the yellow solution was concentrated and injected into the gas chromatograph. 3-Phenyl-1-butene was isolated by preparative gas chromatography (retention time 4.5 min at 100°, column B). The yield was estimated to be 8.5% using gas chromatography with amylbenzene as an internal standard.

Photolysis of PPO in Propylene.—Into a thick-walled Pyrex tube cooled to −78° containing a solution of 300 mg of PPO in 5 ml of acetone was condensed 20 ml of propylene. The tube was carefully sealed under nitrogen and irradiated for 10 hr at room temperature. The yellow solution was filtered, concentrated, and analyzed by gas chromatography on column B at 85°. A single large product was isolated (retention time 4 min) and shown to be allylbenzene by comparison with an authentic sample.

Photolysis of PPO in Butadiene-1,3.—Into a solution of 295 mg of PPO in 5 ml of acetone in a thick-walled Pyrex tube cooled to −78° was condensed 15 ml of butadiene. The tube was sealed carefully under nitrogen and irradiated at room temperature for 8 hr. The yellow solution was concentrated and analyzed by gas chromatography. Two products in the ratio 4:1 were collected and identified as 1,4-dihydronaphthalene (retention time 13 min, 90°, column B) and 1-vinylbenzocyclobutene (retention time 5.5 min). The precise mass measurement for 1-vinylbenzocyclobutene was found to be 130.19243 (calcd for $C_{10}H_{10}$, 130.19126).

Using amylbenzene as an internal standard, the yield of cycloaddition products was found to be 20% by gas chromatography. The irradiation was run identically using tetrahydrofuran in place of acetone as the solvent. The same two products were observed in 4:1 ratio, in addition to the product of reaction of benzyne and tetrahydrofuran.

Photolysis of PPO in Allene.—Into a thick-walled Pyrex tube, cooled to −78°, containing a solution of PPO in 5 ml of acetone was condensed 15 ml of allene. The tube was carefully sealed under nitrogen and irradiated for 8 hr at room temperature. The yellow solution was concentrated and analyzed by gas chromatography. 3-Phenylpropyne (retention time 7 min at 85°, column B) was isolated by preparative gas chromatography and identified by comparison with an authentic sample. Using amylbenzene as an internal standard the yield was determined to be 15%.

Photolysis of PPO in Propyne.—Into a thick-walled Pyrex tube cooled to −78° containing 290 mg of PPO in 5 ml of acetone was condensed 15 ml of propyne. The tube was carefully sealed under nitrogen and irradiated for 10 hr at room temperature. The yellow solution was concentrated and analyzed by gas chromatography. The major component (retention time 8 min at 90°, column B) was identified as phenylallene by comparison with an authentic sample. The yield was determined to be 16% using amylbenzene as an internal standard. An estimated 20% PPO remained.

Photolysis of PPO in Cyclopropane.—Into a thick-walled Pyrex tube, cooled to −78°, containing a solution of 290 mg of

---

[22] We thank the National Science Foundation for providing funds for the purchase of this instrument through Grant GP-5200.

[23] K. E. Russell, *J. Amer. Chem. Soc.*, **77**, 4814 (1955).

PPO in acetone was condensed a large excess of cyclopropane. The tube was carefully sealed under nitrogen and irradiated for 10 hr at room temperature. There was a large amount of polymer so the yellow solution was filtered before concentration and analysis by gas chromatography. Two products in the ratio ~4:1 (retention times 4 and 9 min at 85°, colum B) were observed in addition to several higher boiling components. The major component was identified as allylbenzene by comparison with an authentic sample. It was obtained in 3–4% yield, as determined by using *tert*-butylbenzene as an internal standard. The minor product has not been isolated in sufficient quantity for identification, although it has been established that it is *not* indan.

Registry No.—Benzyne, 462-80-6; PPO, 4733-52-2.

Linear Free-Energy Relationships between Partitioning Solvent Systems[1]

A. LEO* AND CORWIN HANSCH

Department of Chemistry, Pomona College, Claremont, California 91711

Received October 16, 1970

The relationships between the octanol–water partitioning system and 20 others are examined from the viewpoint of the relative contribution of both hydrophobic bonding and hydrogen bonding forces. A classification of solute functional groups according to relative hydrogen-bond donating and accepting ability is presented. Fifty-eight new values for log P octanol–water are reported.

Information on how organic solutes are distributed between water and an immiscible solvent has been of primary interest to chemists working in two different fields: the physical chemist can use the data to help define the intramolecular forces acting between the solute and each of the solvents, and the biochemist can employ it in an approach to structure–activity relationships.[2] In this paper, the relationships between 21 partitioning systems are examined and discussed in reference to their application to both the physical and biological disciplines.

Since, in essence, partition coefficients are equilibrium constants, it should not be surprising that one can find extrathermodynamic relationships[3] between partition coefficients measured in different solvent systems. Certainly such an assumption was implicit in the work of Meyer[4] and Overton[5] who used oil–water partition coefficients to correlate narcotic action of drugs. Later, Smith[6] discussed the possibility of such relationships between two solvent systems if the solute sets chosen were not too dissimilar. Collander[7] was the first to express the relationship clearly in formal terms. Collander showed that a good linear relationship

$$\log P_2 = a \log P_1 + b \qquad (1)$$

existed between partition coefficients in one system (P_1) and those in a second system (P_2) if the polar phase was water and the nonpolar phases contained the same functional group. In particular, he showed that eq 1 held between the systems isobutyl alcohol–water, isopentyl alcohol–water, octanol–water, and oleyl alcohol–water.

Hansch,[8] using Smith's data, later extended the comparison of relatively nonpolar systems using $CHCl_3$–water as P_1 and the following systems for P_2: CCl_4, xylene, benzene, and isoamyl acetate.

While eq 1 allows any partitioning system to be compared with any other, the most useful relationships for the study of solute–solvent interactions are obtained if each system is compared to a standard reference system; that is to say, a reference system should be chosen and made the independent variable P_1 in a set of equations of the form of eq 1.

Of course, objections can be raised to the choice of *any* of the systems for use as a reference standard. We have chosen the octanol–water system for a number of practical reasons: first, it is the system with the largest number of measured values, and it also contains the widest selection of solute functional groups; second, most of these values have been determined in a single laboratory and therefore they are more self-consistent than the values from any other system; and third, the usefulness of the octanol–water system as a model for describing the binding forces between small molecules and macromolecules has already been established.[2]

One might argue that the organic phase in the reference system should be as free of polar binding forces as possible. While in principle a hydrocarbon solvent such as cyclohexane or heptane might make a better reference system than octanol, there are several practical reasons why such a system cannot be constructed at the present time. Of the almost 500 values available in the cyclohexane–water system, a large fraction are for unusual molecules not reported in other systems. Only about 200 values are available in the heptane–water system and these are heavily weighted toward the nonpolar solutes. Furthermore, a basic disadvantage in using a hydrocarbon–water system is that in these solvents dimerization of the solute is maximized. While in principle this factor can be taken into account by measuring the variation of the apparent coefficient with concentration, many of the values reported in the early literature have not been corrected in this manner. Besides it being much more laborious to obtain true partition coefficients in hydrocarbons in which association occurs, the very limited solubility of many polar molecules in these solvents often sets an impossible requirement on the sensitivity of the analytical techniques available.

Another interesting feature of octanol which enhances its value as a partition reference solvent is that, while water is very soluble in it (see Table I), it is very insoluble in water (4.5×10^{-3} M). Thus, in comparison with many of the solvents in Tables I and II, it has relatively little effect on the aqueous phase.

[1] This work was supported by Grant CA-11110 from the National Institutes of Health.

[2] C. Hansch, *Accounts Chem. Res.*, **2**, 232 (1969).

[3] J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963.

[4] H. Meyer, *Arch. Exp. Pathol. Pharmakol.*, **42**, 109 (1899).

[5] E. Overton, "Studien uber die Narkose," Fischer, Jena, Germany, 1901.

[6] H. Smith, *J. Phys. Chem.*, **25**, 204, 605 (1921).

[7] R. Collander, *Acta Chem. Scand.*, **5**, 774 (1951).

[8] C. Hansch, *Farmaco*, **23**, 294 (1968).