Table I shows striking agreement between our directly measured $\Delta F_2°$ values for reaction 2 in acetonitrile solution and corresponding $\Delta F_3°$ values for reaction 3 in aqueous solution. This result then offers compelling confirmation of the H_R acidity function (up to about 50 wt. % acid). The agreement further implies that the free energies to a very major extent measure internal energy effects,[8] i.e., relative cation stabilization energies. The substituent effect on the free energy of solvation of the trityl cation is apparently substantially the same in the aqueous as the non-aqueous solvent (in spite of their great difference in dielectric and other properties), a result which must be attributed to the chemical inertness of the R^+, R–R, and substituent toward the solvent.[3,9,10]

TABLE I
RELATIVE STABILIZATION ENERGIES OF p-SUBSTITUTED TRITYL CATIONS IN ACETONITRILE SOLUTION

p-Subst.	K_{equil}	$-E^0$, v.	$\Delta F_2°$, kcal.	$\Delta F_3°$, kcal.
H, H, H[a]	(1.00)	(0.000)	(0.0)	(0.0)
F, H, H[a]	0.98	.006	0.1	0.1[b]
CH₃, H, H[a]	3.6×10^{-2}	.086	2.0	1.9
OCH₃, H, H[a]	2.0×10^{-4}	.219	5.1	4.4
OCH₃, OCH₃, H[a]	3.7×10^{-8}	.381	8.8	7.4
OCH₃, OCH₃, OCH₃[a]	1.7×10^{-9}	.518	12.0	10.2
N(CH₃)₂, H, H[c]	6.5×10^{-12}	.660	15.2	15.5
N(CH₃)₂, N(CH₃)₂, N(CH₃)₂[c]	3.1×10^{-18}	1.037	23.9	21.8

[a] See ref. 7. [b] Estimated from σ^+ and ρ values listed in ref. 7c. [c] R. J. Goldacre and J. N. Phillips, J. Chem. Soc., 1724 (1949).

The small differences ($\Delta F_2°$ is generally about 10% larger than $\Delta F_3°$) may result from the fact that there is greater localization of the positive charge of R^+ in the C–C than the polar C–O bond. There are also probably some small effects on the $\Delta F°$ values due to symmetry considerations and on $\Delta F_3°$ due to solvation of the OH group.

The ionization potential of organic radicals to cations also has been a quantity of much theoretical interest.[14] The applicability of gas-phase values to chemical reactions in solution is uncertain, however, for reasons of solvation energy as well as of possible excess energy content of the gaseous ions. The great contrast between gaseous ionization potentials of the metallic elements and the corresponding aqueous e.m.f. series serves to illustrate how different in character ionization potentials in the gas and condensed phases can be. Literature values[15] for the equilibrium constants for

(8) L. G. Hepler, J. Am. Chem. Soc., **85**, 3089 (1963).

(9) (a) R. W. Taft, ibid., **82**, 2965 (1960); (b) N. C. Deno, "Equilibria in Concentrated Mineral Acid Solutions," in A. F. Scott's "Survey of Progress in Chemistry," Academic Press, New York, N. Y., 1963; (c) R. H. Boyd, J. Am. Chem. Soc., **85**, 1555 (1963); (d) E. M. Arnett and R. D. Bushick, ibid., in press.

(10) This result may be contrasted with proton transfer equilibria of m- and p-substituted benzoic acids in water[11] and with 1,3-diphenylguanidine in benzene.[12] For m-substituents there is precise fit to the Hammett $\sigma\rho$ relationship, but substituent effects are 230% greater in benzene than water. Further, for $-R$-p-substituents, enhanced resonance effects are observed in water.[13] Evidently, the nonequivalence of substituent effects is to be attributed at least in part to the chemical interactions between solvent and the CO₂H and CO₂⁻ functional groups as well as to different dielectric properties of water and benzene, cf., also, C. D. Ritchie and W. F. Sager, "An Examination of Structure–Reactivity Relationships," in "Progress in Physical Organic Chemistry," 1964, in press.

(11) Ref. 2, Chapter 7.

(12) M. M. Davis and H. B. Hetzer, J. Res. Natl. Bur. Std., **60**, 569 (1958).

(13) R. W. Taft, S. Ehrenson, I. C. Lewis, and R. E. Glick, J. Am. Chem. Soc., **81**, 5352 (1959).

(14) A. Streitwieser, Jr., "Progress in Physical Organic Chemistry," ref. 3, p. 1.

(15) (a) Cf. G. W. Wheland, "Advanced Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 694; (b) J. B. Conant and N. M. Bigelow, J. Am. Chem. Soc., **53**, 676 (1931).

the reaction, $R\cdot + \frac{1}{2}(R_0-R_0) \rightarrow R_0\cdot + \frac{1}{2}(R-R)$, in combination with E^0 values of Table I, provide for the first time quantitative measures of p-substituents on the ionization potentials of trityl radicals in acetonitrile solution. Table II lists the ionization potential data so derived. Unfortunately, gas-phase values (such as those recently reported for benzyl radicals)[16] are not presently available for comparison.

TABLE II
RELATIVE IONIZATION POTENTIALS OF p-SUBSTITUTED TRITYL RADICALS IN ACETONITRILE SOLUTION

p-Subst.	$(I - I_0)$, v.
H, H, H	(0.000)
F, H, H	– .000
CH, H, H	– .043
OCH₃, H, H	– .187
N(CH₃)₂, H, H	– .587

A subsequent detailed report will be made of our e.m.f. cell, as well as the results of studies of the temperature coefficients of the e.m.f. values.

(16) A. G. Harrison, P. Kebarle, and F. P. Lossing, ibid., **83**, 777 (1961).

(17) National Science Foundation Graduate Fellow, 1961–1964.

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RECEIVED OCTOBER 30, 1963

Electronic Interactions in Biradicals. II. A Singlet–Triplet Equilibrium[1,2]

Sir:

We recently reported a study of the radicals derived from 2,2-bis(3,5-di-t-butyl-4-hydroxyphenyl)propane (I). The removal of both phenolic hydrogen atoms of I gave an equilibrium mixture of singlet (bonded) and triplet species. In this case the equilibrium favored the singlet tautomer almost completely. We have modified I in order to make formation of the internal bond more difficult, shifting the equilibrium toward the triplet state. The system we chose is formed by replacing the gem-dimethyl group in I with a 2,2'-biphenylene group, yielding II.

The ordinary (aluminum chloride–carbon disulfide) Friedel–Crafts reaction of 2,6-di-t-butylphenol with 9,9-dichlorofluorene did not appear successful. However, the addition of a solution of silver oxide in acetic acid containing excess perchloric acid to a solution of the phenol and the dichloride in acetic acid produced II in ca. 50% yield, m.p. 272–273° from benzene–hexane.

Anal. Calcd. for $C_{41}H_{50}O_2$: C, 85.66; H, 8.77. Found: C, 85.94, 85.76; H, 8.57, 8.77.

The infrared spectrum of the product was consistent with the assigned structure, λ_{max} 2.7 μ, as was the ultraviolet spectrum, $\lambda_{max}^{C_6H_{12}}$ 299 mμ (log ϵ 2.6), 310 (2.8).

An ethereal solution of the bisphenol (II) was readily oxidized by aqueous alkaline ferricyanide in the usual manner[3] and gave a dark yellow-green solution. Evaporation of the solvent with nitrogen gave a dark oil, which crystallized when treated with pentane. The infrared spectrum (carbon tetrachloride) of this product indicated that both biradical (III) and spirodienone

(1) Paper I: E. A. Chandross and R. Kreilick, J. Am. Chem. Soc., **85**, 2530 (1963).

(2) Partial support (at Washington University) of this work by the U. S. Air Force under contract, the National Science Foundation, the Petroleum Research Fund of the American Chemical Society, and an equipment loan contract with the office of Naval Research is gratefully acknowledged.
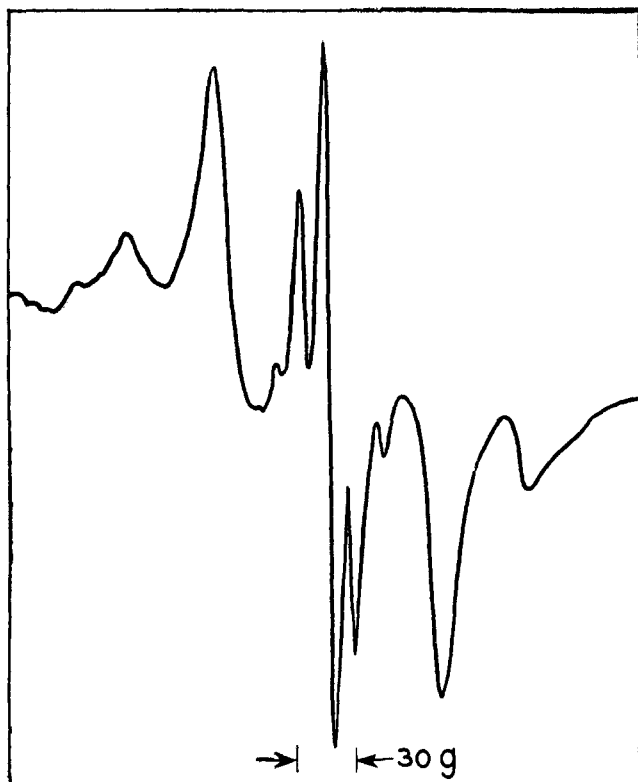
(3) E. Muller and K. Ley, Chem. Ber., **87**, 922 (1954).

Fig. 1.—E.p.r. of II in a rigid glass.

(IV) were present. There are three strong bands in the 6-μ region. The pair of bands at 6.0 and 6.2 μ is assigned to IV, and the band at 6.4 μ is attributed to III. There is ample analogy for these assignments.[3] The oxidation product reacted rapidly with oxygen and gave a mixture of products which was not characterized. The infrared spectrum of the total crude product was consistent with the expected cyclic peroxide being the major component. The optical spectra of solutions of the oxidation products of II were determined at various stages of oxidation but no definitive interpretation could be made.

II   III   IV
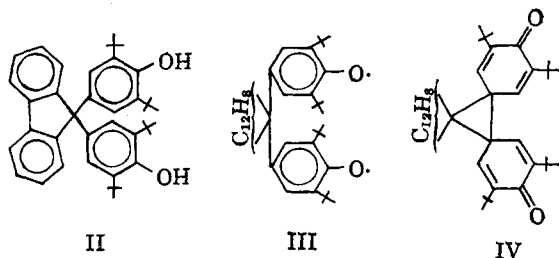
The oxidation of II (methyltetrahydrofuran solution) was also effected by lead dioxide in a sealed, degassed system. The e.p.r. spectrum was monitored as oxidation proceeded. Initially the simple three-line spectrum ($a = 1.65$ gauss) of the monoradical appeared. As oxidation proceeded the intensity of the signal increased and then decreased markedly but it could not be made to vanish entirely. When this solution was frozen to a rigid glass ($ca. -180°$), the e.p.r. spectrum (Fig. 1) revealed the presence of a triplet species. There are two sets of $\Delta m = 1$ lines, about $g = 2$, at ± 63 and ± 15 gauss as well as a half-field ($\Delta m = 2$) absorption. The larger splitting is attributed to biradical III and the smaller to a dimer containing two molecules of III, probably linked by a peroxide bond. Such bond formation would be rather unusual, since phenoxyl radicals bearing three very bulky substituents

are generally thought to be monomeric. An examination of scale molecular models indicated that peroxide bond formation is feasible. The low temperature at which the spectrum was determined would also favor the dimer. This explanation is supported by the concentration dependence of the zero field splitting. Upon dilution the intensity of the smaller splitting decreases much more rapidly than that of the larger and finally disappears completely while the larger splitting is still intense. The positions of these lines indicate that the average distance between electrons in III is 6 Å. while it is 9.8 Å. in the dimer.[4]

The zero field splitting behaved unusually as the sample was heated. The satellite lines decreased in intensity and finally disappeared in the base line. The failure of these lines to reappear as a single broad line at $g = 2$ is attributed to the rapid interconversion of III and IV.

Acknowledgment.—We wish to thank Professor S. I. Weissman for helpful discussions of this work.

(4) G. E. Pake, J. Chem. Phys., 16, 327 (1948).

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Glutarimide Antibiotics. IV. The Total Synthesis of dl- and l-Cycloheximide

Sir:

Cycloheximide (I), a mold metabolite possessing potent fungicidal, antitumor, and rodent-repellent properties, has been the subject of a number of attempted syntheses in recent years.[1-4]

Lack of knowledge of the stereochemistry of cycloheximide and its isomers was a major reason for the failure of these attempts to produce intermediates closely related to I. Clarification of the orientation of the substituents on the cyclohexanone ring of I has recently been forthcoming[5,6] and in conjunction with our own structure studies[6] in this area we have maintained a concurrent synthetic effort. This now has led to the total synthesis of I, reported below.

Catalytic reduction[7] of 2,4-dimethylphenol with palladium on charcoal led directly to cis-2,4-dimethylcyclohexanone[8] (II) which was then converted in excellent yield to the morpholine enamine (III), using a Dowex-50 resin catalyst, b.p. 97–98° (3.0 mm.), $n^{25}D$ 1.4930. *Anal.* Found: C, 73.8; H, 10.7; N, 7.3.

Acylation of III by 3-glutarimidylacetyl chloride (IV) in chloroform followed by decomposition of the intermediate product (V) by means of an acidic buffer led to a 35% yield of dl-dehydrocycloheximide (VI),[6,9] m.p. 180–181°. *Anal.* Found: C, 64.5; H, 7.6; N, 5.2. The solution infrared spectrum of this material was identical with that of dehydrocycloheximide derived

(1) M. A. Acitelli, Ph.D. Thesis, Cornell University, 1957.
(2) B. C. Lawes, J. Am. Chem. Soc., 82, 6413 (1960).
(3) T. Okuda, M. Suzuki, and Y. Egawa, J. Antibiotics (Tokyo), Ser. A, 14, 158 (1961).
(4) F. Johnson, W. D. Gurowitz, and N. A. Starkovsky, Tetrahedron Letters, 1167 (1962).
(5) T. Okuda and M. Suzuki, Chem. Pharm. Bull. (Tokyo), 9, 1014 (1961).
(6) F. Johnson and N. A. Starkovsky, Tetrahedron Letters, 1173 (1962).
(7) The large scale reductions were carried out by W. B. Trapp and H. E. Hennis of the Midland Division of The Dow Chemical Co., and we gratefully acknowledge their assistance.
(8) The product contained 7% of the trans form as estimated by g.l.c. analysis.
(9) The methyl groups in dehydrocycloheximide already have been shown to be trans to one another [A. J. Lemin and J. H. Ford, J. Org. Chem., 25, 344 (1960)].