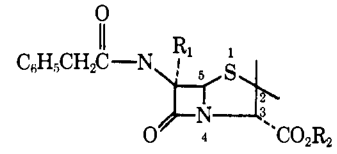
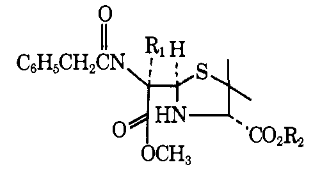


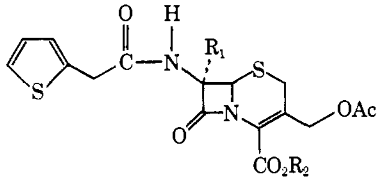
**4a**, $R_1$ = H; $R_2$ = $-CH_2C_6H_4NO_2$
**b**, $R_1$ = H; $R_2$ = H
**c**, $R_1$ = $OCH_3$; $R_2$ = $-CH_2C_6H_4NO_2$
**d**, $R_1$ = $OCH_3$; $R_2$ = H



**5a**, $R_1$ = H; $R_2$ = $-CH_2C_6H_4NO_2$

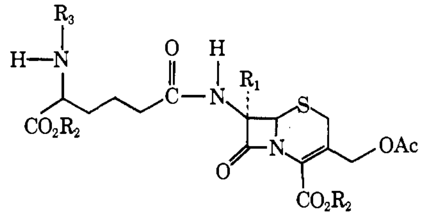
noncrystalline foam:[9,10] ir ($CHCl_3$) 1775, 1745, and 1685 $cm^{-1}$; nmr $\tau$ ($CDCl_3$) $H_5$ 4.41 (s), $H_3$ 5.56 (s), $OCH_3$ 6.60 (s), *gem*-dimethyl 8.70 and 8.50 (s). Hydrogenation of **4c** in methanol–THF using 5% Pd/C gave **4d**.

Having demonstrated the utility of this procedure in the synthesis of 6-methoxypenicillins, we focused our attention on the methoxylation of the cephalosporin molecule. The procedure, by analogy, presented two formidable problems: (1) chlorination at the $C_2$ position and (2) $\Delta^3$ double bond isomerization.[6] However, treatment of **6a** with lithium methoxide (3.5 equiv) and *tert*-butyl hypochlorite at −80° followed by work-up and chromatography gave a 73% yield of **6c**:[11] ir ($CHCl_3$) 1780, 1740, and 1695 $cm^{-1}$; nmr $\tau$ ($CDCl_3$) H 4.93 (s), side-chain methylene 6.09 (s), $OCH_3$ 6.54 (s). The acid (**6d**) was obtained *via* hydrogenation in methanol–THF on 5% Pd/C and converted to its sodium salt **6e** (mp 148–150°).



**6a**, $R_1$ = H; $R_2$ = $-CH_2C_6H_4NO_2$
**b**, $R_1$ = H; $R_2$ = H
**c**, $R_1$ = $OCH_3$; $R_2$ = $-CH_2C_6H_4NO_2$
**d**, $R_1$ = $OCH_3$; $R_2$ = H
**e**, $R_1$ = $OCH_3$; $R_2$ = $Na^+$

It was now apparent that we could confirm the structure of 7-$\alpha$-methoxycephalosporin C (**7e**) obtained by fermentation. Methoxylation of **7b** by the previously described method afforded a 70% yield of **7c**:[12] ir ($CHCl_3$) 1780, 1740, and 1705 $cm^{-1}$; nmr $\tau$ (DMSO-$d_6$) $H_6$ 4.83 (s), $OCH_3$ 6.62 (s), *tert*-butyl 8.63 (s). The synthesis of **7e** was completed by methoxylating **7a**, utilizing the above described conditions, in 65% yield and removing the protecting groups with trifluoroacetic acid–formic acid to give 7-$\alpha$-methoxycephalosporin C in 40% yield.[13,14]



**7a**, $R_1$ = H; $R_2$ = benzhydryl; $R_3$ = *tert*-butyloxycarbonyl
**b**, $R_1$ = H; $R_2$ = $CH_3$; $R_3$ = *tert*-butyloxycarbonyl
**c**, $R_1$ = $OCH_3$; $R_2$ = $CH_3$; $R_3$ = *tert*-butyloxycarbonyl
**d**, $R_1$ = $OCH_3$; $R_2$ = benzhydryl; $R_3$ = *tert*-butyloxycarbonyl
**e**, $R_1$ = $OCH_3$; $R_2$ = H; $R_3$ = H
**f**, $R_1$ = H; $R_2$ = H; $R_3$ = H

**Acknowledgment.** The author is grateful to Dr. R. Nagarajan for kindly supplying us with the natural derivative and would also like to thank Dr. W. H. W. Lunn for useful discussions during this investigation.

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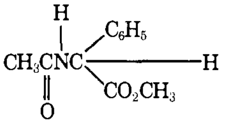
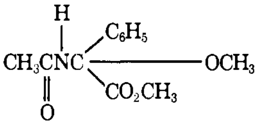
(9) Compound **4c** appears to be more stable to methoxide than the starting penicillin, for treatment of **4b** with 2.5 equiv of lithium methoxide for 15 min afforded a 50% yield of **5a**.

(10) Dr. E. L. Smithwick of Lilly Research Laboratories has demonstrated that under the same conditions, *N*-acetyl-2-phenylglycine methyl ester (i) afforded a quantitative yield of starting material and that, at −20°, one obtained a near quantitative yield of the methoxy amide (ii). These data indicate a reversible O- or N-chlorination followed by dehydrohalogenation. Since the $\alpha$ hydrogen of i is less activated than the $C_6$ hydrogen of penicillin, a higher temperature is required for its proton removal.



i



ii

(11) There was no evidence of double bond isomerization during the reaction.

(12) All spectral data were identical with that of the natural derivative.

(13) The spectral and biological assay data were identical with those of the natural derivative.

(14) For an alternate synthesis of 7e, see R. W. Ratcliffe and B. G. Christensen, *Tetrahedron Lett.*, 2910 (1972).

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## Resonance Energies of Aromatic Hydrocarbons. A Quantitative Test of Resonance Theory

*Sir:*

Molecular orbital (MO) theory has largely supplanted valence bond (VB) theory for quantitative correlations of stability and reactivity. One important reason is the large number of paired electron structures that comprise canonical sets.[1] For example, 429 nonionic structures can be drawn for the $\pi$-electronic system of the relatively small aromatic molecule anthracene. A restriction of VB theory to the simplest structures, *e.g.*, Kekule[2] and Dewar structures, has often been declared to be too inaccurate an assumption for quantitative comparisons.[3]

The crudest variant of VB theory is called resonance theory, in which relative stabilities of isomeric $\pi$-molecular species are deduced from enumeration of Kekule structures alone. This crude but highly

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(1) L. Pauling, *J. Chem. Phys.*, 1, 280 (1933); J. H. Van Fleck and A. Sherman, *Rev. Mod. Phys.*, 7, 167 (1935).

(2) The words "Kekule structure" will refer to any valence bond structure in which single and double bonds alternate.

(3) A. Pullman, *Ann. Chim.* (*Paris*), 2, 5 (1947); P. Daudel and R. Daudel, *J. Chem. Phys.*, 16, 639 (1948); D. P. Craig, *Proc. Roy. Soc., Ser. A*, 200, 272, 390, 401 (1950); C. A. Coulson, *ibid.*, 207, 91 (1951).

Table I. Resonance Stabilization of Aromatic Hydrocarbons

| No. | Compound[a] | VB ($\gamma_1$ units) | HMO ($\beta$ units)[b] | SCF–MO,[c] eV | VB ($\gamma_1$ = 0.838 eV)[d] |
|---|---|---|---|---|---|
| 1 | Benzene | 1.000 | 2.000 | 0.869 | 0.838 |
| 2 | Naphthalene | 1.580 | 3.683 | 1.323 | 1.324 |
| 3 | Anthracene | 1.870 | 5.383 | 1.600 | 1.567 |
| 4 | Phenanthrene | 2.296 | 5.448 | 1.933 | 1.924 |
| 5 | Pyrene | 2.493 | 6.505 | 2.098 | 2.089 |
| 6 | Benzo[*c*]phenanthrene | 2.963 | 7.187 | 2.478 | 2.483 |
| 7 | Benz[*a*]anthracene | 2.709 | 7.101 | 2.291 | 2.270 |
| 8 | Chrysene | 2.963 | 7.192 | 2.483 | 2.483 |
| 9 | Triphenylene | 3.136 | 7.274 | 2.654 | 2.628 |
| 10 | Perylene | 3.160 | 8.245 | 2.619 | 2.648 |
| 11 | Naphthacene | 2.044 | 6.931 | 1.822 | 1.713 |
| 12 | Pentacene | 2.160 | 8.544 | 2.004 | 1.810 |
| 13 | Dibenz[*a*,*c*]anthracene | 3.629 | 8.942 | 3.058 | 3.041 |
| 14 | Dibenz[*a*,*h*]anthracene | 3.493 | 8.881 | 2.948 | 2.927 |
| 15 | Dibenz[*a*,*j*]anthracene | 3.493 | 8.879 | 2.948 | 2.927 |
| 16 | Benzo[*a*]pyrene | 3.102 | 8.222 | 2.854 | 2.599 |
| 17 | Benzo[*d*]pyrene | 3.380 | 8.336 | 2.853 | 2.832 |
| 18 | Benzo[1,12]perylene | 3.581 | 9.425 | 3.128 | 3.001 |
| 19 | Coronene | 4.088 | 10.572 | 3.524 | 3.426 |
| 20 | Benzo[1,14]bisanthene | 4.562 |  | 3.862 | 3.823 |
| 21 | Ovalene | 5.184 | 14.497 | 4.539 | 4.344 |
| 22 | Zethrene | 3.160 |  | 2.694 | 2.648 |
| 23 | Quaterrylene | 6.320 |  | 5.309 | 5.296 |
| 24 | Biphenyl | 2.000 | 4.383 | 1.699 | 1.676 |
| 25 | Styrene | 1.000 | 2.424 | 0.858 | 0.838 |
| 26 | Stilbene | 2.000 | 4.828 | 1.712 | 1.676 |
| 27 | Azulene | 0.370 | 3.363 | 0.169 | 0.310 |
| 28 | Acenaphthylene | 1.580 | 4.619 | 1.335 | 1.324 |
| 29 | Fluoranthene | 2.580 | 6.500 | 2.141 | 2.162 |

[a] Structures of compounds 1–26 are I–XXVI, respectively, given in ref 12. [b] Taken from C. A. Coulson and A. Streitwieser, Jr., "Dictionary of $\pi$-Electron Calculations," W. H. Freeman, San Francisco, Calif., 1965. [c] Reference 12. Corrected values for compounds 5, 16, and 17 (personal communication, M. J. S. Dewar). [d] Average (best fit) value of $\gamma_1$.

useful method is still a ubiquitous component of the pedagogy of organic chemistry.[4] One significant deduction is that compounds for which no Kekule structures can be drawn do not exist.[5] A remarkable quantitative success is the correlation of experimental bond lengths in aromatic hydrocarbons with Pauling bond orders, obtained from unweighted superposings of Kekule structures.[6]

The congruence of resonance theory with many experimental facts has been attributed to good fortune[7] or to unexpected correspondences with results of MO calculations.[8] However, it is a fact that for alternant $\pi$ systems the number of Kekule structures is equal to the product of the eigenvalues of the filled levels (Hückel MO),[8,9] and that both are given by determinants of the same matrix.[10] Therefore, one might surmise that a more complete mathematical relationship exists between simple resonance theory and HMO theory. Platt has discussed this postulate in detail,[11] concluding that the relationship is demonstrated by empirical usefulness of both approximate theories.

A more strict demonstration is a comparison of calculated properties. Since resonance stabilization is an important attribute of aromatic compounds, I decided to calculate resonance energies by VB theory using only Kekule structures and to compare the results with HMO delocalization energies. The results are listed in Table I. A sensitive test for congruity, comparison of resonance energies per $\pi$ electron, is depicted in Figure 1a.

The original hypothesis is not confirmed since resonance theory and HMO theory do not yield precise parallel results. However, the resonance theory calculations do simulate a more complex series of MO calculations, reported by Dewar and de Llano,[12] in

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(4) G. W. Wheland, "Resonance in Organic Chemistry," Wiley, New York, N. Y., 1955.

(5) H. C. Longuet-Higgins, *J. Chem. Phys.*, **18**, 265 (1950); E. Clar, "Polycyclic Hydrocarbons," Vol. 1, Academic Press, New York, N. Y., 1964, Chapter 5.

(6) L. Pauling, L. O. Brockway, and J. Y. Beach, *J. Amer. Chem. Soc.*, **57**, 2705 (1935); D. W. J. Cruickshank, and R. A. Sparks, *Proc. Roy. Soc., Ser. A*, **258**, 270 (1960); D. W. J. Cruickshank, *Tetrahedron*, **17**, 155 (1962).

(7) C. A. Coulson in "Physical Chemistry, An Advanced Treatise," Vol. 5, Academic Press, New York, N. Y., 1970, p 381.

(8) M. J. S. Dewar and H. C. Longuet-Higgins, *Proc. Roy. Soc., Ser. A*, **214**, 482 (1952).

(9) N. S. Ham, *J. Chem. Phys.*, **29**, 1229 (1958).

(10) M. A. Lee, W. C. Herndon, and V. T. Phan, *Acta Mathematica*, submitted for publication.

(11) J. R. Platt, in "Handbuck der Physik," Vol. XXXVII/2, S. Flugge, Ed., Springer-Verlag, Berlin, 1961, pp 187–209.

(12) M. J. S. Dewar and C. de Llano, *J. Amer. Chem. Soc.*, **91**, 789 (1969).

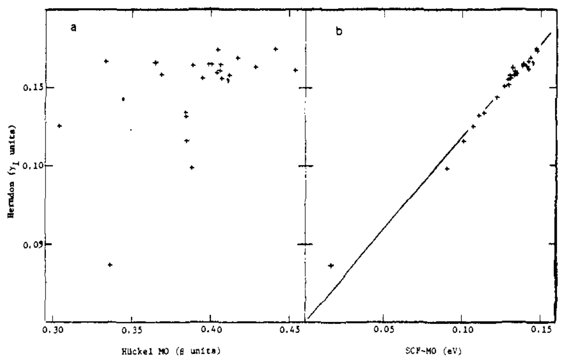

Figure 1. Resonance energies per electron.

which $\pi$ energies are calculated by a semiempirical Pople-type SCF-MO method and in which allowances are made for $\sigma$-bond compression energies (see Table I and Figure 1b). These SCF-MO results probably represent the best estimates of resonance energies available,[13] and the high correlation with the resonance theory values (correlation coefficient is 0.998 for total resonance energy and 0.991 for resonance energy per $\pi$ electron) attests to a utility of the resonance method in calculating resonance energies. Since the formal procedure can be carried out by hand in a few seconds as delineated later in this paper, the simpler theory should be the method of choice for determination of resonance stabilization.

The reasons for the consonant results remain obscure. The VB results are obtained from a method that is little more than a simple recipe, albeit a quantum mechanical recipe. Perhaps the results ought to be accepted in the same pragmatic spirit that HMO results are accepted. Additional work will show whether or not the approach has wider applicability. The results do indicate that VB theory limited to Kekule structures is a viable concept.

Resonance between Kekule structures gives rise to several types of exchange integrals, of which only two are used in this work. $\gamma_1$ refers to resonance between two structures related by a permutation of three bonds within a six-membered ring, and $\gamma_2$ involves the permutation of five bonds within two annelated rings. The resonance energy of benzene is therefore $\gamma_1$ with the lowest energy electronic transition equal to 2.0 $\gamma_1$. The analogous values for azulene are $\gamma_2$ and 2.0 $\gamma_2$. The ratio of $\gamma_2$ to $\gamma_1$ is given by the ratio of the electronic transitions, 7000 and 2600 Å, respectively, $\gamma_2/\gamma_1 = 0.37$.[14] Actual evaluation of the integrals using bond lengths of 1.40 Å gives $\gamma_2/\gamma_1 = 0.36$.[1,15]

The Kekule structures are enumerated by writing a single structure and using the concept of the structure count (SC) as described in a recent paper.[16] One can easily demonstrate that the $\gamma_1$ exchange integrals can then be enumerated by excision of each ring of the structure in turn, with summation of the SC's for the residual systems. The $\gamma_2$ integrals are enumerated by excision of adjacent rings two at a time and application of the same procedure.

The structures are assigned equal weights in the resonance hybrid, and a zero overlap approximation is used. The total resonance energies must then be twice the sum of exchange interactions divided by the number of Kekule structures $K$. Resonance energies are therefore given by the formula RE $= 2(n_1\gamma_1 + 0.37n_2\gamma_2)/K$.

**Acknowledgment.** The financial support of the Robert A. Welch Foundation is gratefully acknowledged. Useful discussions with D. M. Lee are greatly appreciated.

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*Received December 18, 1972*

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[13] See the papers by B. A. Hess, Jr., and L. J. Schaad for a different viewpoint, *J. Amer. Chem. Soc.*, **93**, 305, 2413 (1971); *J. Org. Chem.*, **36**, 3418 (1971).

[14] S. P. McGlynn, L. G. Vanquickenborne, M. Kinoshita, and D. G. Carroll, "Introduction to Applied Quantum Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1972, pp 214-217.

[15] C. A. Coulson and W. T. Dixon, *Tetrahedron*, **17**, 215 (1962).

[16] W. C. Herndon, *Tetrahedron*, **29**, 3 (1973).

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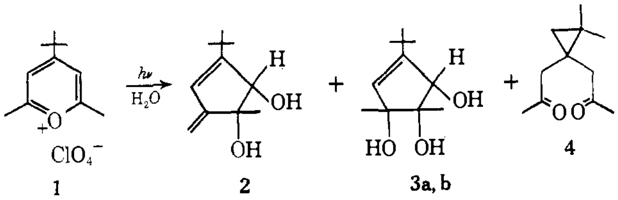
## Photochemistry of 4-*tert*-Butyl-2,6-dimethylpyrylium Perchlorate. Evidence for an Oxoniabenzvalene Intermediate

*Sir:*

We wish to report a study of the photochemistry of 4-*tert*-butyl-2,6-dimethylpyrylium perchlorate (**1**), the products from which provide strong evidence for the intermediacy of an oxoniabenzvalene, *i.e.*, an oxygen analog of benzvalene.

Irradiation of the pyrylium salt **1** in water (λ >270 nm; 25°; nitrogen atmosphere; 0.02 *M* solution; 18 hr) gave an acidic solution from which an oil was isolated by ether extraction. Chromatography of the oil on silica gel gave four main products, **2**, **3a**, **3b**, and **4**, in yields of 4, 15, 2, and 6%, respectively. Under the conditions described, *ca.* 70-80% of the pyrylium salt was destroyed. The structural assignments are based on the following evidence.



The diol **2**, mp 71-72°, $C_{11}H_{18}O_2$, had $\tau$ ($CDCl_3$)[1] 4.06, 5.08, 5.13 (each 1 H, apparent s), 5.94 (1 H, d, $J$ = 7 Hz; collapsed to s on $D_2O$ exchange), 7.33 (OH, d, $J$ = 7 Hz), 7.4 (OH, s), 8.75 (3 H, s), and 8.84 (9 H, s).

Triol **3a** crystallized as the hemihydrate $C_{11}H_{20}O_3 \cdot 0.5H_2O$, mp 60-61°, which had $\tau$ ($CDCl_3$)[1] 4.39 (1 H, s), 5.97 (1 H, d, $J$ = 6 Hz; collapsed to s on $D_2O$ exchange), 6.53 (OH, s), 7.58 (OH, d, $J$ = 6 Hz), 7.69 (OH, s), 8.41 (OH, s), 8.79 (3 H, s), and 8.88 (12 H, s).

Triol **3b** mp 150.5-151°, $C_{11}H_{20}O_3$, had nmr ($CDCl_3$)[1] $\tau$ 4.47 (1 H, s), 5.62 (1 H, d, $J$ = 7 Hz; collapsed to s on $D_2O$ exchange), 7.49 (OH, s), 7.82 (OH, d, $J$ = 7 Hz), 8.39 (OH, broad), 8.62 (3 H, s), 8.72 (3 H, s), and 8.86 (9 H, s).

**3a** and **3b** were both converted into **2**, identical in all

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[1] The chemical shifts for the OH signals in **2**, **3a**, and **3b** were concentration dependent. The quoted values are for *ca.* 1% solutions. At higher concentrations, the OH resonances collapsed to a single broad peak.