

methylindole from *o*-acetotoluide in a yield of 85% of the theoretical, and mentions that indole can be prepared from *o*-formotoluide and recommends the use of a diluent.

Madelung² used sodium alkoxides as condensing agents on various toluides to prepare 2-substituted indoles, including 2-methylindole but reports failure to isolate any indole from attempts to condense *o*-formotoluide.

The author was unsuccessful in preparing indole in satisfactory yields by the use of sodium amide, monoxide, or alkoxides on *o*-formotoluide. However, by the use of potassium or potassium amide in liquid ammonia, or potassium ethoxide, or methoxide, or *t*-butoxide, essentially pure indole can be prepared readily in yields as indicated in the following table.

YIELDS OF INDOLE PER MOLE OF <i>o</i> -FORMOTOLUIDE				
Potassium cpd. used	Molar ratio of potassium cpd.	Indole, g.	<i>o</i> -Toluidine recovered, g.	Yield, % ^a
Potassium in liquid ammonia	1.0	30	..	51
Amide in liquid am- monia	1.0	28	..	48
Methoxide	1.0	37	53	63
Ethoxide	1.0	37	52	63
Ethoxide	1.5	40	..	68
<i>t</i> -Butoxide	1.0	41	50	70
<i>t</i> -Butoxide	1.5	46	..	79

^a These yields are calculated on the assumption that 2 moles of formotoluide are required theoretically for the production of 1 mole of indole. The extra mole of formotoluide can be accounted for almost quantitatively as isolated toluidine.

Sufficient of the absolute alcohol for the solution of potassium was placed in a three-necked Pyrex flask connected for reflux, and the apparatus was filled with nitrogen gas. The potassium was added in convenient portions with external cooling. The required *o*-formotoluide was added and the condenser was set for distillation. The excess alcohol was removed by distillation with the aid of a metal bath, and the residue heated to 350–360° for twenty minutes. During this twenty minute interval, combustible gas was evolved, chiefly carbon monoxide and hydrogen, and liquid was condensed from which *o*-toluidine was recovered upon redistillation.

Water was added, after cooling, to the residue in the flask, and the mixture was steam distilled until indole ceased to come over. The distillate was ether extracted, the ether extract was treated with cold dilute (5%) hydrochloric acid, water, and dilute sodium carbonate (5%) solution and dried over sodium sulfate. Upon removal of ether, and distillation under reduced pressure, essentially pure indole was obtained; b. p. 128° (10 mm.), m. p. 53°.

The potassium amide was prepared in liquid ammonia, and the *o*-formotoluide was added to the liquid ammonia

(2) Madelung, *Ber.*, **45**, 1130 (1912).

solution, with subsequent treatment essentially as described above.

Numerous experiments with higher molecular properties of the above-mentioned potassium compounds and at various temperature ranges resulted in no improvement in yields.

Attempts to prepare indole by the use of sodium amide with or without solution in liquid ammonia, or by the use of a diluent such as diethylaniline or kieselguhr resulted in practically negligible yields of indole; the same result was obtained when sodium monoxide was used as the condensing agent. Attempts to substitute sodium ethoxide, or methoxide, or *t*-butoxide for the corresponding potassium compounds were likewise unsuccessful.

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The Resonance Energies of Unsaturated and Aromatic Molecules

By G. W. WHELAND

Mulliken and Rieke¹ have shown that, in the approximate quantum mechanical treatment of molecules by the molecular orbital LCAO method, the usual assumption^{2,3,4} of orthogonality between adjacent atomic orbitals is not necessary. In the special case in which the integrals⁵ α , β , γ and S are considered to be constant, the procedure of these authors can be put into a somewhat simpler, but equivalent form, in the following manner. When the non-orthogonality integral S is included, the energy of the i th molecular orbital is given by

$$E_i = \frac{\alpha + n_i \gamma}{1 + n_i S}$$

where n_i is a numerical constant obtained by solution of the same secular equation that is used when $S = 0$. This expression for E_i is too complicated as it stands to be easily used, but it is changed by the substitution

$$n_i = \frac{m_i}{1 - m_i S}$$

(1) R. S. Mulliken and C. A. Rieke, *THIS JOURNAL*, **63**, 1770 (1941).

(2) E. Hückel, *Z. Elektrochem.*, **43**, 752, 827 (1937).

(3) G. W. Wheland, *J. Chem. Phys.*, **2**, 474 (1934).

(4) J. E. Lennard-Jones, *Proc. Roy. Soc. (London)* **A158**, 280 (1937).

(5) The notation used here is that of Mulliken and Rieke.¹ The quantities α , γ , and E have been previously called α , β and w , respectively, by Hückel,² and q , β and w , respectively, by Wheland.³ In addition, Lennard-Jones⁴ has used the symbol δ for the present S , and he has had somewhat different expressions for α and γ .

into

$$E_i = \alpha + m_i(\gamma - \alpha S) \equiv \alpha + m_i\beta$$

When all of the E_i 's are expressed in this manner, the resonance or conjugation energy becomes a multiple of the single parameter β , just as it was a multiple of γ in the treatment of Hückel, Wheland and Lennard-Jones. Moreover, the results of the calculations made by that earlier, less rigorous method can be immediately corrected without the necessity of solving any further secular equations;

this is done by merely replacing γ by $\beta = \gamma - \alpha S$ and n_i by $m_i = n_i/(1 + n_i S)$ for each root of the previously solved equations.

It is of interest to see to what extent the results of the calculations corrected in the above manner are consistent with the experimental thermal data and with the results of the earlier valence bond and molecular orbital calculations. Such a comparison is made for a series of unsaturated and aromatic hydrocarbons in Table I and for a series

TABLE I
RESONANCE ENERGIES OF UNSATURATED MOLECULES

Compound	Resonance Energy			J (kcal. per mole)	γ (kcal. per mole)	β (kcal. per mole)	J/β	β/γ	
	Empirical ^a (kcal. per mole)	Valence bond treatment ^a	Molecular orbital treatment (uncor.) ^a						Molecular orbital treatment (cor.)
Benzene	36	-1.11J	-2.00 γ	-1.07 β	-33	-18	-34	0.96	1.87
Biphenyl	87	-2.37J	-4.38 γ	-2.25 β	-37	-20	-39	.95	1.95
Naphthalene	75	-2.04J	-3.68 γ	-1.86 β	-37	-20	-40	.91	2.01
Anthracene	105	-5.31 γ	-2.61 β	..	-20	-40	..	2.03
Phenanthrene	110	-5.45 γ	-2.74 β	..	-20	-40	..	2.00
Pyrene	-6.51 γ	-3.21 β	2.03
Styrene	46	-1.31J	-2.42 γ	-1.21 β	-35	-19	-38	.92	2.00
Stilbene	94	-2.59J	-4.88 γ	-2.45 β	-36	-19	-38	.94	1.99
1,1-Diphenyl- ethylene ^b	89	-2.55J	-4.81 γ	-2.40 β	-35	-19	-37	.94	2.00
1,3,5-Triphenyl- benzene	182	-4.77J	-9.15 γ	-4.62 β	-38	-20	-39	.97	1.98
Butadiene	3.6 ^c	-0.32J	-0.47 γ	-0.17 β	-11	-8	-21	.53	2.76
Fulvene	...	-0.50J ^d	-1.47 γ	-.64 β	1.28	2.30
Azulene	...	-1.14J ^d	-3.36 γ	-1.60 β	1.40	2.10
Cyclobutadiene	...	-1.00J	0.00	+0.53 β	-0.53	0.00

^a Cf. G. W. Wheland³ and further references given there. A few figures are taken from unpublished calculations of the author. The letter J here represents the single exchange integral between adjacent atomic orbitals; it was called α by Wheland in the reference given. ^b This substance was incorrectly called iso-stilbene by Wheland.³ ^c G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith and W. E. Vaughan, THIS JOURNAL, **58**, 146 (1936). ^d A. L. Sklar, J. Chem. Phys., **5**, 669 (1937).

TABLE II
FREE RADICAL RESONANCE ENERGIES OF RADICALS^a

Radical	Free Radical Resonance Energy			J/β	β/γ
	Valence bond treatment ^b	Molecular orbital treatment (uncor.) ^b	Molecular orbital treatment (cor.)		
Phenylmethyl	-0.51J	-0.72 γ	-0.40 β	0.79	1.80
<i>m</i> -Biphenylmethyl	-.51J	-.72 γ	-.40 β	.79	1.80
β -Naphthylmethyl	-.63J	-.74 γ	-.47 β	.75	1.57
<i>p</i> -Biphenylmethyl	-.65J	-.76 γ	-.44 β	.68	1.73
α -Naphthylmethyl	-.75J	-.81 γ	-.53 β	.71	1.53
Fluoryl	-.80J	-1.34 γ	-.78 β	.98	1.71
Diphenylmethyl	-.84J	-1.30 γ	-.69 β	.82	1.88
Phenylfluoryl	-1.08J	-1.84 γ	-.99 β	.92	1.86
Triphenylmethyl	-1.11J	-1.80 γ	-.92 β	.83	1.96
Tri- <i>m</i> -biphenylmethyl	-1.11J	-1.80 γ	-.92 β	.83	1.96
Diphenyl- <i>p</i> -biphenylmethyl	-1.17J	-1.82 γ	-.93 β	.79	1.96
α -Naphthyl-diphenylmethyl	-1.24J	-1.86 γ	-1.01 β	.81	1.84
Tri- <i>p</i> -biphenylmethyl	-1.29J	-1.86 γ	-0.97 β	.75	1.92

^a The free radical resonance energy is defined as the resonance energy of the radical minus the resonance energy which would obtain if the odd electron were held on the methyl carbon atom. It is thus a measure of the extent to which the resonance stabilizes the radical with respect to the ethane. ^b Cf. ref. *a*, Table I.

of free radicals in Table II. In the corrected molecular orbital calculations, S was assumed to have the rounded-off value of 0.25. It is seen that the agreement of the various calculations with experiment and with each other is excellent in most cases, as is shown by the approximate constancy of the values of J , γ and β , and of the ratios J/β and β/γ . The discrepancies with butadiene (Table I) are presumably due to the fact that, with such a small effect, the complications arising from further factors, such as a lack of constancy of the integrals J , α , β , γ and S , the alterations in bond distances, etc., are relatively very important. The obviously impossible result that the resonance energy of cyclobutadiene is negative (Table I), which is obtained in the corrected molecular orbital calculation, is to be related to the fact, previously pointed out,⁶ that the molecular orbital treatment of this molecule does not take into account the resonance between the two Kekulé-like structures. With the free radicals (Table II) the calculated orders of increasing free radical resonance energy are in most cases the same as the observed order of increasing dissociation of the corresponding ethanes. While the valence bond treatment seems to reproduce the experimental order somewhat more satisfactorily in some regards than either of the molecular orbital treatments, there are too many further, unconsidered factors, such as solvent effects, entropy changes, steric effects, etc., to permit a judgment as to which of the three treatments is really the most accurate. This is especially true in view of the smallness of the differences involved. It is interesting that none of the methods accounts for the observed greater dissociating effect of the *m*-biphenyl group⁷ as compared with the phenyl group.

The conclusion to be reached from the above discussion is that, in cases like those considered, the explicit inclusion of the integral S in the molecular orbital treatment makes no significant difference in the self-consistency of the calculations of resonance energies of molecules, or of free radical resonance energies of radicals. There is no assurance, however, that the same will be true in the calculations of any other properties, especially in those cases in which the integrals α , β , γ and S cannot be considered constant. In fact, Mulliken and Rieke¹ have found that the

(6) G. W. Wheland, *Proc. Roy. Soc. (London)*, **A164**, 397 (1938).

(7) C. S. Marvel, E. Ginsberg and M. B. Mueller, *THIS JOURNAL*, **61**, 77 (1939).

explicit inclusion of S does materially improve the agreement of the calculations with the spectroscopic data. The fact that the value of the integral β is about twice that of γ also seems to be an improvement, since the old figure of $\gamma \simeq -20$ kcal. per mole was hard to reconcile either with the known bond energies or with the ultraviolet absorption spectra of the molecules.

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NEW COMPOUNDS

α -Guanido- γ -methylmercaptobutyric Acid (Guanidomethionine)

The method employed for the preparation of this compound was similar to that reported for guanidocystine.^{1,2} To a solution of 0.74 g. of *dl*-methionine in 10 cc. of 0.5 *N* potassium hydroxide was added 1.04 g. of methyl-isothiurea hydriodide. The solution was put into a vacuum desiccator which was then evacuated for five hours. After a total of fourteen hours in the desiccator under reduced pressure the dried crystals were dissolved in 10 cc. of water. As before, this solution was slowly brought to dryness in the vacuum desiccator. The dried crystals were rubbed well with 30 cc. of acetone containing 6 drops of concentrated ammonia. Potassium iodide is soluble in acetone in the presence of ammonia. The crystals were filtered off, washed with two 5-cc. portions of ammoniacal acetone, then with plain acetone and air dried. The crude guanidomethionine was obtained as white crystals in about 92% yield. The Sakaguchi reaction was positive. After 3 recrystallizations from boiling water it was obtained as six-sided plates; dried in an Abderhalden apparatus, m. p. 193–194°.

Anal. Calcd. for $C_6H_{13}N_3SO_2$: N, 21.99. Found: N, 21.78.

(1) J. Kapfhammer and H. Müller, *Z. physiol. Chem.*, **225**, 1 (1934).

(2) Jesse P. Greenstein, *J. Biol. Chem.*, **112**, 35 (1935–1936).

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5-Iodo-7-bromoisatin and 2-Amino-3-bromo-5-iodobenzoic Acid

5-Iodo-7-bromoisatin.—A solution of 3 g. of 5-iodoisatin in 100 ml. of ethyl alcohol was heated to boiling under reflux and 5 g. of bromine added slowly. The reaction mixture was maintained at reflux temperature for eight hours, after which most of the alcohol was removed. The prod-