Calculation of the π-Electron "Ring Current" Properties of Some Carcinogenic, Heptacyclic, Condensed, Benzenoid Hydrocarbons

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Calculations are reported on the π-electron "ring current" properties of several carcinogenic, condensed, benzenoid hydrocarbons, containing 7 rings. The "ring current" theory has recently been shown to account very satisfactorily for the observed chemical shifts in a wide range of benzenoid molecules, and these calculations are presented as a reliable aid to future analyses of the experimental pmr spectra of these hydrocarbons; these spectra may, in turn, throw light on the electronic distribution in these molecules, often thought to be involved in their carcinogenic effects. Trends in the calcd ring current intensities and proton chemical shifts are discussed, with particular reference to the corresponding values of these quantities obtained in previous calcns on the smaller carcinogens of this type. The present calcns complement this earlier work, with the result that ring current data are now available on *all* the *planar*, polycyclic, condensed, benzenoid hydrocarbons, which have so far been shown to be carcinogenically active.

In the past decade, considerable effort has been devoted to the study and calculation of the nmr properties of condensed, benzenoid hydrocarbons,[1-16] mostly for the purpose of testing the validity of MO theories,[1-4,8,9,11,13,16,20] but also partly[1,5,6,11-13,16] in the hope of shedding light on the electronic distribution in these molecules, which has been thought to influence their carcinogenic activity.[21] Experimental and theoretical study has so far been confined, however, to the smaller and more familiar classic carcinogens—such as benzo[*a*]pyrene,[1,2,6,9,11-13,15] benz[*a*]anthracene,[1,5,7,8,12-15] and dibenz[*a,h*]anthracene[1,2,6,9,12-15]—with some theoretical consideration to the hexacyclic carcinogens.[16] Now, Buu-Hoï and coworkers[18,19,22,23] have drawn attention to the fact, that hydrocarbons derived from naphthacene (such as I–III), as well as large "hypercondensed"[18] hydrocarbons (such as IV and V), can also have carcinogenic properties; benzo[*a*]naphtho[2,1,8-*hij*]naphthacene (I) produces sarcomas by sc injection,[18,19] as does[22] benzo[*a*]naphtho[8,1,2-*cde*]naphthacene (II), while tribenzo[*a,c,j*]naphthacene (III), although not sarcomagenic *in situ*, has produced leukemias and ovarian tumors;[18] of the two symmetrical heptacyclic carcinogens considered, dibenzo[*h,rst*]pentaphene (IV) (with C_{2v} symmetry) is a relatively potent sarcomagen,[18,23] while dibenzo[*cd,lm*]perylene [peropyrene (V)] (D_{2h} symmetry) is a much milder one.[22]

In view of the fact that semiempirical MO theory has recently been shown[15] to account very satisfactorily for the π-electron magnetic properties of polycyclic, condensed, benzenoid molecules, we present here calculations of the magnetic effects arising from the induced π-electron ring currents in these 5 "unorthodox"[18] carcinogens. It is intended that these will be of future use in analyzing the experimental pmr spectra of these hydrocarbons; in the case of I–III, it is likely, in view of previous experience with other molecules of only C_{1h} symmetry,[11,12,14,20] that it will not be possible to obtain complete analyses from spectra recorded at field strengths of less than 220 MHz.

Calculations.—The calculations reported in Tables I and II were performed using McWeeny's modification[24] of London's gauge-invariant LCAO–MO method,[25] for describing the magnetic effects due to π-electron ring currents in aromatic molecules. The McWeeny theory has been discussed in detail elsewhere;[24,1-3,8,9,15,16,20] for our purposes here we merely note that it affords an entirely quantum mechanical method of predicting, not only the relative secondary magnetic fields produced, by the "mobile" π electrons, at the various constituent protons, but also the individual ring current intensity in each ring of a polycyclic molecule. In the light of experience gained in previous cal-

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TABLE I

RING CURRENT INTENSITIES (RELATIVE TO THE INTENSITY OF THE RING CURRENT IN BENZENE) IN MOLECULES I TO V

Compd	Ring current intensity in rings A	B	C	D	E	F	G
Benzo[*a*]naphtho-[2,1,8-*hij*]naphthacene (I)	1.139	0.932	1.366	1.263	0.824	1.288	1.092
Benzo[*a*]naphtho-[8,1,2-*cde*]naphthacene (II)	1.141	1.355	1.136	0.559	1.038	1.234	1.096
Tribenzo[*a,c,j*]naphthacene (III)	1.122	0.886	1.294	1.232	0.628	1.071	1.070
Dibenzo[*h,rst*]pentaphene (IV)	1.184	1.161	1.183	0.508	1.022		
Peropyrene (V)	1.332	1.031	1.446				

culations,[15] it was considered justifiable to represent molecules I–V as networks of regular hexagons, of side equal in length to the C–C bond length in benzene (0.139 nm), with all C–H bond lengths equal to 0.108 nm, and to select a unique resonance integral, β for all aromatic C–C bonds, irrespective of their environment. The calculations were performed using a version of the program[15,16,20] NPRC, modified for the Oxford University KDF 9 computer.

Results and Discussion

(a) π-Electron Ring Current Intensities.—Table I shows the calcd ring current intensities (expressed relative to the magnitude of the ring current in benzene) in molecules I–V. The smallest ring current so far calcd in a condensed, benzenoid hydrocarbon is 0.236 [in benzo[*b*]perylene (XXI) of ref 16], and the largest in a polycyclic molecule of 7 rings or less[3b] is 1.460 (in the outer rings of coronene[3,4]); it is seen from Table I that all the ring currents in I–V fall (just) within this range. It had also previously been observed[16] that the more condensed a given ring is, the smaller the π-electron ring current it bears appears to be. In I–IV this rule is justified up to a point (Table I), but a dramatic exception is the central ring in peropyrene (V) which has a ring current intensity of 1.446—over *6 times* that (0.239) in the (formally) analogous central ring in perylene[15] (which is similarly condensed with 4 surrounding rings), and nearly as high as that calcd[3,4] for the outer rings of coronene (1.460). This is at first sight, a surprising difference, but it can be rationalized by the well-known fact[26] that the central bonds in perylene, connecting the two naphthalenic units, never appear other than as *single* bonds in any of the several Kekulé structures which can be devised for the molecule as a whole; in peropyrene, however, there is no such "bond fixation" [in the valence bond–resonance theory[27] (VB–RT) sense of this term] and hence, in this molecule, *all* bonds in the central ring necessarily participate fully in the conjugation between the upper and lower halves of the molecule.[28] One can thus appreciate, albeit somewhat heuristically, an intuitive, physical reason for the observation of a very small ring current intensity in the central ring of perylene, and a much larger one in the (apparently) analogous central ring of peropyrene. The apparent correlation between *increase* in the extent of VB–RT bond fixation and *decrease* in the intensity of MO π-electron ring currents will be discussed in more detail, with reference to further examples, elsewhere.[29]

TABLE II

CALCULATED RING CURRENT DESHIELDING (RELATIVE TO THE DESHIELDING IN BENZENE) AT THE VARIOUS NONEQUIVALENT PROTONS IN MOLECULES I TO V

Compd	Proton	σ ratio[a,b]	Proton	σ ratio[a,b]	Proton	σ ratio[a,b]	Proton	σ ratio[a,b]
Benzo[*a*]naphtho[2,1,8-*hij*]naphthacene (I)	1	1.641	2	1.476	3	1.599	4	1.285
	5	1.332	6	1.897	7	2.070*	8	1.647*
	9	1.296	10	1.266	11	1.406	12	1.306
	13	1.403	14	2.085*	15	1.769*	16	1.566
Benzo[*a*]naphtho[8,1,2-*cde*]naphthacene (II)	1	1.587	2	1.436	3	1.645*	4	1.453*
	5	1.192	6	1.202	7	1.515*	8	1.847*
	9	1.922	10	1.509	11	1.287	12	1.290
	13	1.527	14	2.052*	15	1.737*	16	1.547
Tribenzo[*a,c,j*]naphthacene (III)	1	1.528*	2	1.222	3	1.206	4	1.428*
	5	1.428*	6	1.206	7	1.219	8	1.520*
	9	1.872*	10	1.832	11	1.309	12	1.240
	13	1.371	14	1.240	15	1.269	16	1.601*
	17	1.963*	18	1.889*				
Dibenzo[*h,rst*]pentaphene (IV)	1	1.689*	2	1.351	3	1.335	4	1.537
	5	1.789*	6	1.475*	7	1.182	15	1.772*
Peropyrene (V)	1	1.698	2	1.540	4	1.541	5	1.729*

[a] σ ratio is $H'/H'_{benzene}$. See text. [b] Asterisk indicates a proton subject to steric hindrance. See text.

With regard to comparison of the ring current intensities reported here, with those calcd previously in smaller (and, in general, more potent) carcinogens of analogous structure, it is of interest to observe that I can be thought of as a benzo[*a*]pyrene molecule perturbed by the addition of rings A and B; it is then pertinent to note that the ring currents in rings D, E, F, and G in I (1.263, 0.824, 1.288, and 1.092, resp) follow closely those calcd[1] for the corresponding rings in benzo[*a*]pyrene itself (1.280, 0.840, 1.292, and 1.077). Similarly, II can be regarded as being formed from the carcinogen,[16b] naphtho[2,1,8-*qra*]naphthacene,[16] with the additional condensation of ring E; the ring current intensities in rings A, B, F, and G of II then compare respectively with those (given in parentheses) in the

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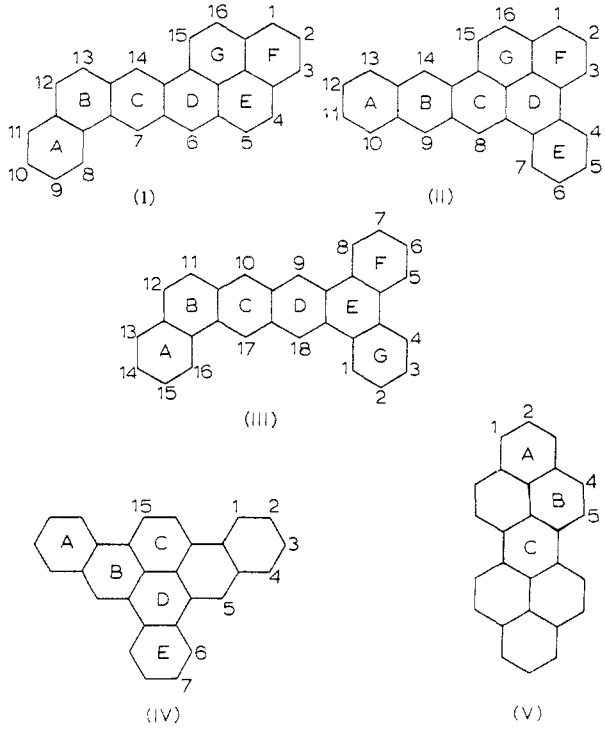
corresponding rings of the parent hexacyclic molecule, as follows: 1.141 (1.143), 1.355 (1.372), 1.234 (1.268), 1.096 (1.089). Furthermore, ring currents in rings C, D, E, F, and G of III compare with those found in the analogous rings of dibenzo[*a*,*c*]naphthacene,[16c] thus: 1.294 (1.311), 1.232 (1.194), 0.628 (0.603), 1.071 (1.061), 1.070 (1.061). Finally, ring current intensities in rings A, B, and C of dibenzo[*h*,*rst*]pentaphene (IV) follow closely those of the corresponding rings of the potent carcinogen,[16] benzo[*rst*]pentaphene (IX in ref 16a)—1.184 (1.191) for ring A in IV, and its analog, 1.161 (1.214) for ring B, and 1.183 (1.181) for ring C.

These comparisons therefore emphasize the fact, that small perturbations brought about by condensation of additional rings in one region of a large polycyclic hydrocarbon *may* often have only a second-order effect on the ring current intensities in rings *distant* from the site of the perturbation, though this is by no means always the case.[29] Hence, we see that ring current intensities in these large, novel, and "unorthodox"[18] carcinogens are, in fact, very similar in magnitude to those encountered in the smaller classic carcinogens, of analogous structure.

(b) Proton Chemical Shifts.—Table II lists the calcd secondary magnetic fields (H′), due to the π-electron ring currents, at the various constituent protons in these molecules; again, these are expressed as a ratio to the deshielding, secondary field ($H'_{benzene}$), calcd to arise at a benzene proton, on account of the ring current in benzene. The σ ratios[15,16] ($H'/H'_{benzene}$) are related to the chemical shifts of the individual constituent protons, and, by using the empirically established[15] regression equation

$$\tau_{calcd} = -1.56(H'/H'_{benzene}) + 4.34 \qquad (1)$$

these σ ratios can be converted into calcd chemical shifts (at infinite dilution[15] in CCl_4), on the τ scale. In eq 1, the constant term embodies, empirically, all the contributions to the proton chemical shifts from the anisotropy of the σ bonds (both C–C and C–H)—a contribution which has been shown[15] to change very little on going from a benzene proton to protons in a *general* polycyclic benzenoid molecule. The term in ($H'/H'_{benzene}$) thus accounts for the chemical shift contribution from the ring current effect. The ($H'/H'_{benzene}$) ratios (Table II) are typical of those found in smaller carcinogens,[8,9,15,16] with those protons near the centers of molecules experiencing the largest ring current deshielding (*e.g.*, 7 and 14 in I, and 14 in II, all with σ ratios greater than 2.0). The protons identified with an asterisk in Table II are involved in proton–proton steric interactions, similar to those occurring in phenanthrene;[15,30] in addition, therefore, to receiving chemical shift contributions from the σ and π electrons predicted by eq 1, the pmr signals from such overcrowded protons are expected[4,8-11,15,16,20] to be displaced about 0.6 ppm further downfield (resulting in a *lower* τ value), as a consequence of these steric effects.



The calculations reported here complement earlier work[1-4,8,9,15,16] on the smaller molecules of this type, with the result that ring current data are now available on *all* the *planar*, polycyclic, condensed, benzenoid hydrocarbons which have so far been shown to be carcinogenically active. I–V are, in fact, the largest known carcinogens of this series, and it is perhaps surprising[18] that such activity is manifested in spite of the general low solubility of planar systems having more than 6 benzene rings. As Buu-Hoï has observed[18] however, there is no reason to believe that even the degree of condensation displayed in I–V represents an upper limit for carcinogenic activity; furthermore, molecules of these dimensions are of particular significance when considering theories which require a potential carcinogen to have a supposedly "optimum" geometry for successful attack on cell components.

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