259. Electrostatic Potential Field and Nucleophilicity of 3, 5, 8, 10-Tetramethyl-aceheptylene

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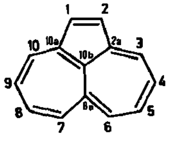
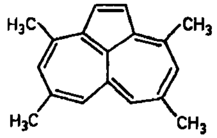
(16. IX. 75)

Summary. The electrostatic potential (EP.) for aceheptylene (I) is calculated using *ab-initio* wavefunctions. In addition, the EP. around I is approximated by a monopole expression, using wavefunctions from various semiempirical procedures as a basis. It is found that the previously noted discrepancy between the theoretical prediction of differential nuclophilicity of the individual unsaturated C-atoms in 3,5,8,10-tetramethyl-aceheptylene(II) and the experimental results of protonation is removed, if instead of local atomic charges, the EP. around II, approximated by that of I is considered.

Introduction. – In a previous communication it was shown using various methods that semi-empirical calculations of the charge distribution in aceheptylene (I) led to a rather non-uniform picture [1]. Given the fact that the local atomic charges (AC) have served many times in the past as theoretical indices for predicting the behaviour of molecules on attack by charged reagents, a clarification of this matter was considered essential, especially in view of the intriguing reactivity pattern shown by the related System II on attack of a proton leading to III, IV and V [1] [2].



I



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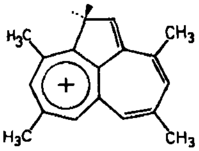

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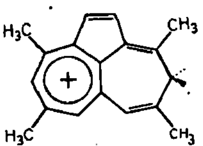
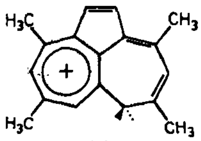


IV



V

In a first attempt to rectify the issue we tried to get 'experimental' insight into the charge distribution of II *via* known correlations between local AC's and ^{13}C-chemical shifts [1]. The outcome of this investigation turned out to be inconclusive

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and thus did not allow us to decide about the 'relative reliability' of the various semi-empirical procedures in calculating useful charge distributions.

Experience shows that considerations of local atomic charges as reactivity indices do not always lead to satisfactory results. A nice example of this is provided by the *para*-directing effect of fluorine in electrophilic substitution reactions of fluorobenzene [3]. It was shown recently that the use of more sophisticated reactivity indices such as the over-all electrostatic potential (EP) [4] around the molecule saves the situation in this case [5], whereas a consideration of AC's indicates the *meta*-position as the most favourable substitution site.

The limited usefulness of computed AC's for the prediction of chemical properties is related to the fact that they do not correspond to observable quantities. Their values therefore necessarily suffer from a certain amount of ambiguity. We decided therefore to investigate the electrostatic potential around I, assuming it to be a good model system for II.

Theoretical Procedure. – It has been found for quite a number of cases [5] [12] that electrostatic potentials computed from non-empirical (*ab initio*) wavefunctions are capable of discriminating between the reactivity of similar systems or reaction sites. Hence, we embarked on a non-empirical SCF/LCAO/MO calculation.

The basis set used for I consisted of 254 primitive Gaussians: 7 s-type and 3 p-type functions for carbon [7] and 3 s-type functions for hydrogen [8]. This basis was contracted to a minimal basis set of 80 functions. The calculations were performed with the program MOLECULE [9] using the mean of the molecular geometry parameters reported for II in [10] and [11] as determined by X-ray diffraction.

Results and Discussion. – In Table 1 the *ab initio* gross atomic populations of I are listed together with corresponding values obtained from some ZDO semi-empirical calculations. From this it becomes evident that the former do not point toward C(1) as being the most nucleophilic of the three relevant C-atoms C(1), C(4) and C(6), at variance with the experimental findings for II [2]. (It has already been pointed out before [1] that the same finding also applies to the results of most of the semi-empirical SCF-procedures mentioned in Table 1).

Fig. 1 shows the molecular isopotential map obtained for a plane parallel to the molecule at a distance of 1.75 Å. In a previous study of benzene [12] the potential minima were found to be located at this distance above the molecular plane. A similar distance, corresponding roughly to half the 'thickness' of a planar π-system, can also be deduced from the EP.-maps of some heteroatomic systems depicted in [4].

Two regions of potential minima are clearly discernible: The deepest around the 5-ring bond C(1)–C(2) (−24 kcal/mol), the other roughly above C(4) (−16 kcal/mol). The EP. above C(6) lies only around −10 kcal/mol. These data suggest that the most favorable 'electrostatic' channel for an incoming electrophile leads ultimately to its covalent bonding at C(1), in agreement with the experimental finding that III is the exclusive primary protonation product of II [2]. During equilibration of the system IV accumulates, the corresponding EP. of I around C(4) indeed being second in magnitude. Finally at thermodynamic equilibrium only V is present, the corresponding lowest relative rate of electrophilic attack being in agreement with the highest relative EP. around C(6) of I.

It has been pointed out that a calculation of the electrostatic interaction of a proton with a base yields values which are numerically much smaller than experi-

Table 1. *Atomic electron populations from various semi-empirical procedures and from present* ab initio *calculation.* (For references concerning the semi-empirical methods consult [1].)

	HMO	*Lo-Whitehead* a)	*Chung-Dewar* a)	*Dewar-Harget* a)	*Yamaguchi* a)	PPP/CI a)	CNDO/2 b)	MINDO/3 b)	*ab initio* c)
C(1)	1.122	1.032	1.046	1.038	1.063	1.068	4.033	4.031	6.216
C(2a)	1.091	1.081	1.111	1.086	1.076	1.082	4.036	4.055	6.055
C(3)	0.882	0.901	0.841	0.891	0.923	0.899	3.931	3.907	6.152
C(4)	1.049	1.076	1.125	1.084	1.049	1.057	4.055	4.079	6.239
C(5)	0.899	0.911	0.859	0.901	0.938	0.921	3.924	3.893	6.169
C(6)	1.048	1.073	1.121	1.079	1.035	1.057	4.051	4.085	6.209
C(6a)	0.884	0.861	0.822	0.853	0.893	0.893	3.886	3.843	5.973
C(10b)	0.934	0.987	0.971	0.990	0.945	0.940	3.970	3.981	5.978
H—C(2)							1.015	1.007	0.814
H—C(3)							1.003	1.009	0.781
H—C(4)							1.009	1.004	0.804
H—C(5)							1.005	1.014	0.780
H—C(6)							1.010	1.005	0.807

a) ZDO-SCF-π-procedures, atomic electron densities.

b) ZDO-SCF-all valence electron-procedures, atomic electron densities.

c) Gross atomic populations.

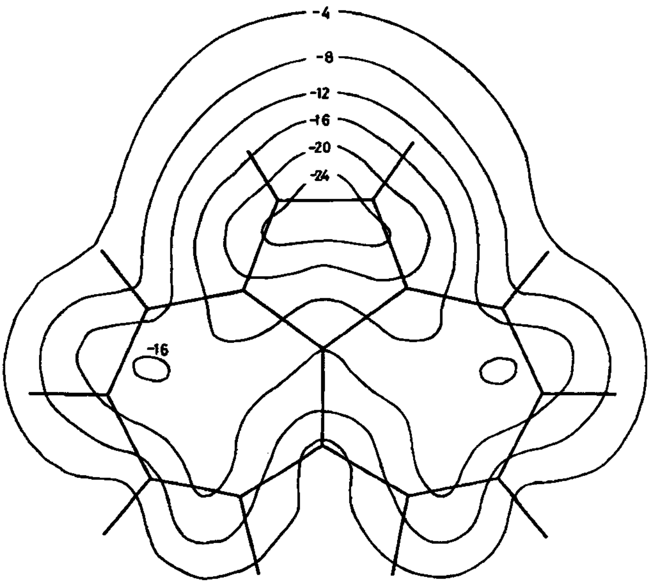

Fig. 1. *Electrostatic isopotential map for aceheptylene* (I), *drawn 1.75 Å above the molecular plane* (see text). Contour values in kcal/mol

mentally determined proton affinities [4]. Clearly covalent bonding can not be rationalized only on electrostatic grounds. But experience shows that the ratio between real proton affinities and electrostatic interaction energies is approximately constant for a wide series of protonation processes [4], thus allowing at least a rough ordering scheme. The present example however does not obey this correlation in two respects:

a) The potential minimum for benzene was found to be −14.2 kcal/mol [12], *i.e.* deeper than that around C(6) of I. Experimentally II is a much stronger base than benzene, given that the thermodynamically most stable V is formed even in dilute aqueous sulfuric acid. It must be emphasized, though, that a more flexible basis set was used in [12]. Indeed, test calculations have shown that the EP. obtained from *ab initio* calculations may vary considerably for different choices of small and medium-sized basis sets [15]. To make a comparison between EP.'s for different molecules strictly meaningful, basis sets of the same quality should be used. Even if such is the case, however, it must be borne in mind that several factors in addition of proton affinity determine the basicity of a molecule in solution.

b) Within I itself there is also clearly no correlation between computed EP.'s and basicity: While EP.(C(1)) < EP.(C(4)) < EP.(C(6)), experimentally pK_a(V) > pK_a(IV) > pK_a(III) is observed [2]. Note that this 'non-correlation' indeed is the crux of the matter since it discloses the 'EP.-index' as a satisfactory tool for predicting the kinetically controlled reactivity of II.

As a corrollary of the *Bell-Evans-Polanyi* principle [13] reactions exhibiting kinetic control involve early transition states, the reaction partners being well separated from each other at that stage. At such distances interaction between them is therefore predominantly of long-range electrostatic nature, polarization or charge-transfer effects playing only a minor role. Hence for such reaction types the 'EP.-index' is truly appropriate.

It should be noted that the 'EP.-index' has also been successful in predicting correctly a kinetically controlled primary protonation process in the case of pyrrole [4].

Table 2. Ab initio *orbital energies* (eV) *for aceheptylene* (I) (see text)

	$-\varepsilon$(eV)		$-\varepsilon$(eV)		$-\varepsilon$(eV)
$3a_2(\pi)$	8.53	$19a_1(\sigma)$	17.41	$8b_2(\sigma)$	29.93
$4b_1(\pi)$	10.29	$14b_2(\sigma)$	18.41	$11a_1(\sigma)$	30.74
$2a_2(\pi)$	12.17	$18a_1(\sigma)$	18.73	$7b_2(\sigma)$	31.98
$3b_1(\pi)$	12.95	$13b_2(\sigma)$	19.13	$10a_1(\sigma)$	32.47
$18b_2(\sigma)$	14.78	$17a_1(\sigma)$	19.81	$9a_1(\sigma)$	34.16
$2b_1(\pi)$	14.83	$16a_1(\sigma)$	21.06	1s(C(1), C(2))	309.90
$1a_2(\pi)$	14.93	$12b_2(\sigma)$	21.32	1s(C(2a), C(10a))	310.56
$17b_2(\sigma)$	15.52	$11b_2(\sigma)$	21.69	1s(C(4), C(9))	310.64
$22a_1(\sigma)$	15.60	$15a_1(\sigma)$	22.36	1s(C(6), C(7))	310.85
$21a_1(\sigma)$	15.99	$10b_2(\sigma)$	24.24	1s(C(3), C(10))	311.57
$16b_2(\sigma)$	16.49	$14a_1(\sigma)$	24.94	1s(C(10b))	311.63
$20a_1(\sigma)$	16.70	$13a_1(\sigma)$	26.61	1s(C(5), C(8))	311.71
$1b_1(\pi)$	16.94	$9b_2(\sigma)$	27.51	1s(C(6a))	312.74
$15b_2(\sigma)$	17.25	$12a_1(\sigma)$	28.76		

For allowing comparison to be made with possible future calculations, the *ab initio* orbital energies for I are also given below in Table 2. The roughly equidistant spacings between the first three π-MO's compare favorably with those obtained from the positions of the first three well resolved peaks in the photoelectron spectrum of II with $IP_1 = 6.55$ eV, $IP_2 = 7.63$ eV and $IP_3 = 8.53$ eV [14], although the absolute experimental values as well as the absolute spacings associated with them are smaller. This is due to the well known errors inherent in *Koopmans'* theorem as well as use of the minimal basis set. Furthermore, introduction of the four alkyl groups in I leading to II will result in a decrease of all IP's due to inductive and/or hyperconjugative stabilization of its radical ion states. Considering these points the agreement between calculation and experiment is qualitatively satisfactory. Note that IP_1 (II) is among the lowest IP's ever observed for hydrocarbons of this size. The present calculation leads to –534.02603 a.u. for the total energy of I.

Reactivity indices from semi-empirical calculations. The EP.-map drawn above for I was obtained using the proper expression for the EP. at a point P, which in the case of LCAO-expanded wavefunctions is

$$\mathrm{EP.(P)} = \sum_{\mathrm{N}}^{\mathrm{Nuclei}} \frac{Z_{\mathrm{N}}}{R_{\mathrm{NP}}} - \sum_{\mathrm{i,j}}^{\mathrm{Basis}} P_{\mathrm{ij}} \int \frac{\varphi_{\mathrm{i}}\varphi_{\mathrm{j}}}{r_{\mathrm{P}}}\, d\tau. \tag{1}$$

Here the first term comprises the EP. due to the nuclear charges, the second term the EP. arising from the electron distribution $P_{ij}\varphi_i\varphi_j$. Various approximations to this second term have been proposed and carefully compared with each other [16]. However, we thought it worthwhile to seek an approximation which does not necessitate additional programming work but which can be applied by the average user of quantum chemical programs on the basis of standard program output only. With this aim in mind, the monopole approximation to the EP.

$$\mathrm{EP.(P)} = \sum_{\mathrm{N}}^{\mathrm{Nuclei}} \frac{Q_{\mathrm{N}}}{R_{\mathrm{NP}}} \tag{2}$$

was tried with Q_N = net charge at atom N.

Experience from calculations applying (1) shows that EP.-minima for π-Systems are often situated vertically above particular nuclei, the associated distance being usually around 2 Å. Therefore we have positioned the points P (*e.g.* the proton positions) vertically above C(1), C(4) and C(6) and have calculated EP.(P) for values of R_{NP} varying between 1 Å and 5 Å. The results obtained from the different semi-empirical procedures (= different Q_N-sets) are given in Table 3, together with the results of the same calculation using the gross atomic populations of the present *ab initio* calculation. It can be seen that on this basis all procedures yield the prediction that electrophilic attack is clearly preferred at C(1), leading to III. Furthermore, all semi-empirical procedures indicate that C(4) should be slightly more nucleophilic than C(6). Note that this predicted sequence of nucleophilicity does not depend on R_{NP}, thus increasing the significance of the approximation (2).

Conclusion. – Attempts to correlate the observed reactivity of II with individual atomic charges met with difficulties since the latter differ with regard to their sequence of magnitude across a spectrum of calculatory procedures. Consideration of the EP. around II, properly calculated or even grossly approximated on a monopole basis yields, however, a unifying picture in complete agreement with experiment.

Table 3. *Monopole-approximated electrostatic potential* (EP. in eV) *at 1–5 Å above C(1), C(4) and C(6) of I, using five different sets of wavefunctions* (see text)

		EP. at C(1)	EP. at C(4)	EP. at C(6)
5 Å	*ab initio*	– 0.366	– 0.271	– 0.304
	MINDO/3	– 0.029	0.029	0.052
	CNDO/2	– 0.031	0.034	0.062
	PPP/CI	– 0.091	0.024	0.057
	HMO	– 0.158	0.046	0.108
4 Å	*ab initio*	– 0.530	– 0.388	– 0.439
	MINDO/3	– 0.054	0.044	0.080
	CNDO/2	– 0.057	0.051	0.094
	PPP/CI	– 0.150	0.044	0.090
	HMO	– 0.261	0.080	0.167
3 Å	*ab initio*	– 0.801	– 0.595	– 0.657
	MINDO/3	– 0.111	0.069	0.129
	CNDO/2	– 0.115	0.079	0.148
	PPP/CI	– 0.270	0.082	0.147
	HMO	– 0.467	0.147	0.265
2 Å	*ab initio*	– 1.322	– 1.044	– 1.061
	MINDO/3	– 0.250	0.094	0.200
	CNDO/2	– 0.255	0.110	0.232
	PPP/CI	– 0.545	0.145	0.235
	HMO	– 0.927	0.272	0.440
1 Å	*ab initio*	– 2.805	– 2.548	– 2.270
	MINDO/3	– 0.633	– 0.094	0.082
	CNDO/2	– 0.649	– 0.008	0.225
	PPP/CI	– 1.291	0.098	0.217
	HMO	– 2.182	0.366	0.582

Though II is a non-alternant hydrocarbon in which usually considerable charge migrations are found to occur, the present example suggests that even in such cases predictions based on single AC's are to be taken with due caution.

Multipole expansions of the EP. for a neutral compound involve as the leading term a dipolar contribution. In this respect it is noteworthy that the negative end of the permanent dipole of I, calculated from all the charge distributions given in Table 1, is always situated near the 5-membered ring, and the electrical center of gravity is found to be always slightly displaced from the mid-point of the C(1)–C(2) bond toward that region. Hence, already dipole moment considerations yield the unifying result that the nucleophilicity of II is greatest at the 5-membered ring atoms.

This work is part of project No. 2.8250.73 of the «*Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung*». *E.H.* and *F.J.* acknowledge financial support by *Ciba-Geigy SA*, *Hoffmann-La Roche SA* and *Sandoz SA*. *J.A.* and *J.K.* gratefully acknowledge support from the *Swedish Natural Science Research Council.*

REFERENCES

[1] *H. Fritz, E. Haselbach & F. Jachimowicz*, submitted for publication.

[2] *E. Haselbach*, Tetrahedron Letters *1970*, 1543; *W. Friebe*, Dissertation TH Darmstadt 1973; *F. Jachimowicz*, Dissertation University of Basel 1975; *W. Friebe*, K. *Hafner*, *E. Haselbach*, *F. Jachimowicz & P. Seiler*, in preparation.

[3] *W.A. Sheppard & C.M. Sharts*, 'Organic fluorine chemistry', Benjamin, New York 1969.

[4] *E. Scrocco & J. Tomasi*, Fortschritte chem. Forschung *42*, 95 (1973).
[5] *J. Almlöf, A. Henriksson-Enflo, J. Kowalewski & M. Sundbom*, Chem. Physics Letters *21*, 560 (1973).
[6] *R.C. Bingham, M.J.S. Dewar & D.H. Lo*, J. Amer. chem. Soc. *97*, 1285 (1975).
[7] *B. Roos & P. Siegbahn*, Theoret. chim. Acta *17*, 209 (1970).
[8] *S. Huzinaga*, J. chem. Physics *42*, 1293 (1965).
[9] *J. Almlöf*, USIP Report 74 – 29 (Dec. 1974).
[10] *E. Carstensen-Oeser & G. Habermehl*, Angew. Chem. *80*, 564 (1968).
[11] *R. Quasba, F. Brandl, W. Hoppe & R. Huber*, Acta crystallogr. *B 25*, 1198 (1969).
[12] *J. Almlöf, H. Johansen, B. Roos & U. Wahlgren*, J. Electron Spectrosc. *2*, 51 (1973).
[13] *M.J.S. Dewar*, 'The Molecular Orbital Theory of Organic Chemistry', *Wiley*, New York 1969.
[14] *E. Haselbach & F. Jachimowicz*, unpublished results.
[15] *J. Almlöf & Å. Støgård*, Chem. Physics Letters *29*, 418 (1974).
[16] *C. Giessner-Prettre & A. Pullman*, Theoret. chim. Acta *25*, 83 (1972).

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260. Anwendung von Ringerweiterungen zur Herstellung von *rac*-Muscon und Exalton®1)

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(25. VIII. 75)

Application of Ring Expansions for the Preparation of *rac*-Muscone and Exaltone®.

Summary. 4,6-Undecamethylene-2-pyrone (**8**), prepared from 1-morpholino-cyclododec-1-ene (**7**) according to *Hünig et al.*, was saponified and decarboxylated to a mixture of the 3-methyl-cyclotetradecenones **11**, **12**, **13** and **14**, which was hydrogenated to 3-methyl-cyclotetradecanone (**3**). Similarly, 4,6-dodecamethylene-2-pyrone (**16**) was prepared from 1-morpholino-cyclotridec-1-ene (**15**) and ketene, saponified to a mixture of the 3-methyl-cyclopentadecenones **19**, **20**, **21** and **22** and the latter hydrogenated to *rac*-muscone (**6**).

The ratios of the four regio- and stereoisomers in the above mentioned two mixtures of 3-methyl-cycloalkenones were derived from the ^{1}H-NMR.-spectra.

From the reactions of the enamines **7** and **15** were also isolated small amounts of 4,5-decamethylene- (**9**) and 4,5-undecamethylene-6-methyl-2-pyrone (**17**) respectively. Saponification and partial decarboxylation of **9** lead to (2-acetyl-cyclododec-1-enyl)-acetic acid (**23**) and methyl-(2-methyl-cyclododec-1-enyl)-ketone (**24**), the latter possessing an incense-like odor.

The keton homologation method of *Mock & Hartman* (reaction of alkanones with diazoacetic ester in the presence of triethyl oxonium fluoroborate, followed by saponification and decarboxylation) was applied three times in succession, starting with cyclododecanone (**1**). This furnished, after the first stage, the cyclotridecanone (**4**) required for the above described synthesis of *rac*-muscone (**6**) and, after the third stage, cyclopentadecanone (**5** = exaltone®).

Application of this reaction to 2-methyl-cyclododecanone (**28**) resulted in a low yield of 2-methyl- (**30**) and 3-methyl-cyclotridecanone (**31**) in the ratio of 2:1.

1. Einleitung. – Wir beschreiben hier eine Methode zur Umwandlung des leicht zugänglichen [1] Cyclododecanons (**1**) in 15gliedrige Ringketone, wie z.B. die Riechstoffe [2] Exalton® (**5**) und *rac*-Muscon (**6**). Sie besteht aus zwei Reaktionsfolgen (a und b), zusammenfassend in *Schema 1* dargestellt.

Die erste Reaktionsfolge (a) ist eine Weiterführung der Enamin-Keten-Ringerweiterung [3]; sie erlaubt die Herstellung des übernächsten Homologon mit gleichzeitiger Einführung einer Methylgruppe in β-Stellung zur Carbonylfunktion (**1** → **3** und

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1) Aus der geplanten Dissertation von *Martin Karpf*. Vorgetragen an der Versammlung der Schweizerischen Chemischen Gesellschaft am 11. Oktober 1974 in Neuenburg.