A Theoretical Investigation of the Effect of Positively Charged Substituents on Product Distribution in Electrophilic Aromatic Substitution; Evidence for a Dominant Field Effect of the Positive Poles

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Ab initio (STO-3G) molecular orbital calculations of energy changes associated with *meta*- and *para*-protonation of the ions $C_6H_5\cdot[CH_2]_n\cdot NN_3^+$ show that the deactivating and *meta*-directing properties of positively charged substituents upon electrophilic aromatic substitutions are primarily due to the field effect of the pole. Classical electrostatic calculations of energies of interaction between the substituent and the positive charges on the protonated phenyl ring closely reproduce the results of the molecular orbital calculations, confirming the importance of field effects.

THERE is a continuing interest in the effect of positively charged substituents upon product distribution in electrophilic aromatic substitutions.[1] In general it is found that positive poles are *meta*-directing and deactivating groups.[2] Available evidence indicates that this is primarily due to the field effect rather than the σ-inductive effect of the substituent.[1] However, conjugative (resonance) interactions may also be important, particularly when the positive pole is directly attached to the phenyl group.[1]

It has recently been shown that *ab initio* calculations at the STO-3G level of approximation [3] can be used to predict substituent effects upon electrophilic aromatic substitution.[4] It had been demonstrated previously that semi-empirical (CNDO/2) calculations provide information about the ability of positive poles to polarize aromatic π-electron systems.[5] Consequently we decided to carry out *ab initio* (STO/3G) calculations of electrophilic aromatic substitution for the system $C_6H_5\cdot[CH_2]_n\cdot NH_3^+$ ($n = 0$—2). The purpose was twofold: to elucidate further the origin(s) of the substituent effect of positive poles on electrophilic aromatic substitution, and to obtain information on the π-polarization effect of positive poles.

RESULTS AND DISCUSSION

Calculations were carried out for the isodesmic reaction [4,*] (i). Only *meta*- and *para*-attack were considered since the proportion of *ortho*-products is generally small for reactions of this kind.[2]

Energy changes for reaction (i) are summarized in Table 1. Data are included for $C_6H_5[CH_2]_nNH_3^+$ ($n = 0$—2) and for a C_6H_6, NH_4^+ pair with the ammonium ion in the same position as the NH_3^+ group in the phenethylammonium ion.† The calculation for this last case was carried out in an attempt to confirm the

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† Geometries used in the calculations are given in the Details of Calculations section.

[1] J. H. Rees, J. H. Ridd, and A. Ricci, *J.C.S. Perkin II*, 1976, 294.

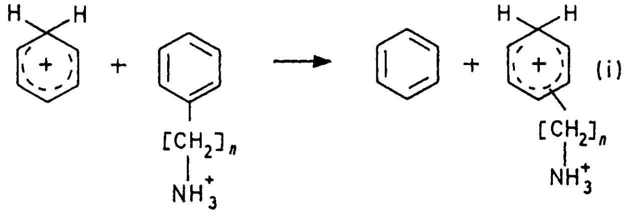
[2] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' 2nd edn., Bell, London, 1969, ch. VI.

[3] W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, 1969, **51**, 2657.

[4] J. M. McKelvey, S. Alexandratos, A. Streitwieser, J.-L. M. Abbovd, and W. J. Hehre, *J. Amer. Chem. Soc.*, 1976, **98**, 244.

[5] W. F. Reynolds, I. R. Peat, M. H. Freedman, and J. R. Lyerla, *Canad. J. Chem.*, 1973, **51**, 1857.

existence of a through-space electric field effect on electrophilic aromatic substitution (elimination of the alkyl link removes the possibility of σ-inductive and conjugative effects). The energy changes are compared



* This is the reverse of the reaction given in ref. 4. We chose to define the energy change in this direction in order to allow direct comparison with electrostatic calculations of the interactions between positive charges.

with product distribution for nitration of the derivatives $C_6H_5[CH_2]_n{\cdot}N(CH_3)_3^+$ in sulphuric acid (see Table 1). The trimethylammonio-derivatives were chosen since product distributions for ammonio-derivatives vary markedly with acid concentration, suggesting significant solvation effects.[6] The trimethylammonio-groups should be less strongly solvated than NH_3^+ and thus more closely resemble a positive pole in the gas phase [although the $N(CH_3)_3^+$ group is also significantly solvated (see below)]. Comparison of stabilities of Wheland intermediates with product distributions makes the normal assumption of a parallel between activation energy and intermediate stability.

TABLE 1

Calculated energy changes for reaction (i) and the electrostatic energy of interactions between positive charges in ring-protonated compounds $C_6H_5{\cdot}[CH_2]_n{\cdot}NH_3^+$ compared with orientation in nitration for $C_6H_5{\cdot}[CH_2]_n{\cdot}N(CH_3)_3^+$

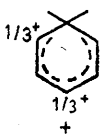
System (R = H or CH_3)	Calculation type (for R = H)	Energy (kcal mol^{-1})		Product composition (%) for nitration of $C_6H_5{\cdot}[CH_2]_n{\cdot}N(CH_3)_3^+$	
		meta	*para*	*meta*	*para*
$C_6H_5{\cdot}NR_3^+$	MO	106.1	110.4	89	11 [a]
	Electrostatic	114.5	133.2		
$C_6H_5{\cdot}CH_2{\cdot}NR_3^+$	MO	85.8 (87.8) *	87.6 (96.1) *	88	10 [b]
	Electrostatic	89.4	94.2		
$C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}NR_3^+$	MO	66.5 (68.9) *	64.0 (73.9) *	16	78 [c]
	Electrostatic	64.9	66.4		
C_6H_6,NH_4^+	MO	64.9	65.6		
	Electrostatic	64.9	66.4		

* Corrected for alkyl group effects (see text).

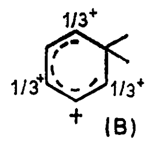
[a] M. Brickman, J. H. P. Utley, and J. H. Ridd, *J. Chem. Soc.*, 1965, 6851. [b] F. R. Gross, W. Hanhart, and C. K. Ingold, *J. Chem. Soc.*, 1927, 250. [c] A. Ricci and J. H. Ridd, *J.C.S. Perkin II*, 1972, 1544.

The calculated relative stabilities of *meta*- and *para*-protonated Wheland intermediates closely parallel the product distribution, reproducing the change from predominant *meta*-substitution to *para*-substitution between $n = 1$ and $n = 2$. However, the calculations for the C_6H_6,NH_4^+ pair indicate that the *meta*-protonated intermediate is favoured in this case. This shows that the greater stability of the *para*-protonated intermediate (and the lower experimental activation energy for *para*-attack) in the phenethylammonium ion is due to the electron-releasing effect of the alkyl group, as previously suggested.[1] Streitwieser *et al.*[4] have reported data for the effects of methyl and ethyl groups on stabilities of *meta*- and *para*-protonated intermediates {respectively −2.0 and −8.5 kcal mol^{-1} for CH_3 and −2.4 and −9.7 kcal mol^{-1} for CH_2CH_3 [same sign convention as in (i)]}. If one substracts these alkyl group effects for benzylammonium ion and phenethylammonium ion, then the residual effect for the ammonium pole is *meta*-directing in each case.

The usual explanation for the *meta*-directing effect of a positive pole is that charge repulsion between the positive pole and the positive charge at C-1 [see (A)] disfavours the *para*-intermediate (and transition state).[7] To check this picture and to compare with the theoretically calculated energies, the electrostatic energy of interaction between a unit positive charge and a unit positive charge distributed equally on the three indicated carbon atoms was calculated for the various positions of the nitrogen pole. Results are summarized in Table 1. There is nearly quantitative agreement between the results of this classical electrostatic calculation and the energy differences from the molecular orbital calculation. The agreement is not quite as good at close range as at long range. Although this might in part be due to the failure to include a term for the dielectric constant of the molecular framework,[8] it is most likely due primarily to the fact that the localized charge molecule used in the electrostatic calculation is an oversimplification (see below). In any case, the good agreement between the two calculations provides strong support for the conclusion that the *meta*-directing properties of positive poles are due to field effects.



(A)



(B)

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[6] S. R. Hartshorn and J. H. Ridd, *J. Chem. Soc.* (*B*), 1968, 1063.

[7] R. O. C. Norman and R. Taylor, ' Electrophilic Substitution n Benzenoid Compounds,' Elsevier, Amsterdam, 1965, ch. 2.

[8] J. G. Kirkwood and F. W. Westheimer, *J. Chem. Phys.*, 1938, **6**, 508.

The calculated charge densities are summarized in Table 2. They indicate that protonation of the benzene ring results in considerable charge delocalization in the σ-electron system. However, there are large π-electron density changes almost identical to that shown in (A) and (B). This undoubtedly accounts for the near quantitative agreement of molecular orbital and electrostatic calculations. However, the former calculations also indicate that the positive charge on the substituent is primarily located on the hydrogen atoms (*ca.* +0.35 charge units on each).* This has the effect of increasing the charge separation between the positive pole and the ring. This may account for the overestimation of the field effect in the anilinium ion by the electrostatic calculations since these calculations assumed that the positive charge was on the nitrogen atom.

TABLE 2

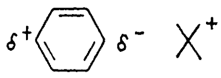
Calculated total charge density and (in parentheses) π-charge density for phenyl groups in $C_6H_5{\cdot}[CH_2]_n{\cdot}NH_3^+$ (relative to benzene) and changes in charge density upon ring protonation

	$C_6H_5NH_3^+$	*para*-Protonated $C_6H_5{\cdot}NH_3^+$	*meta*-Protonated $C_6H_5{\cdot}NH_3^+$		$C_6H_5{\cdot}CH_2{\cdot}NH_3^+$	*para*-Protonated $C_6H_5{\cdot}CH_2{\cdot}NH_3^+$	*meta*-Protonated $C_6H_5{\cdot}CH_2{\cdot}NH_3^+$
C-1	+0.141	+0.150	+0.003	C-1	+0.037	+0.145	−0.005
	(−0.164)	(+0.340)	(−0.024)		(−0.092)	(+0.353)	(−0.026)
C-2	+0.014	−0.022	+0.149	C-2	+0.002	−0.022	+0.146
	(+0.013)	(−0.075)	(+0.330)		(+0.007)	(−0.074)	(+0.332)
H-2	+0.024	+0.059	+0.075	H-2	+0.006	+0.058	+0.074
C-3	+0.025	+0.162	−0.110 [a]	C-3	+0.013	+0.156	−0.104 [a]
	(+0.031)	(+0.364)			(+0.023)	(+0.345)	
H-3	+0.043	+0.080	+0.100	H-3	+0.028	+0.078	+0.101
C-4	+0.036	−0.128 [a]	+0.151	C-4	+0.024	−0.116 [a]	+0.150
	(+0.074)		(+0.337)		(+0.052)		(+0.330)
H-4	+0.045	+0.101	+0.079	H-4	+0.032	+0.100	+0.079
C-5	+0.025	+0.162	−0.016	C-5	+0.013	+0.156	−0.016
	(+0.031)	(+0.364)	(−0.064)		(+0.023)	(+0.345)	(−0.062)
H-5	+0.043	+0.080	+0.062	H-5	+0.028	+0.078	+0.065
C-6	+0.014	−0.022	+0.136	C-6	+0.002	−0.022	+0.140
	(+0.013)	(−0.075)	(+0.321)		(+0.007)	(−0.074)	(+0.318)
H-6	+0.024	+0.059	+0.087	H-6	+0.006	+0.058	+0.088

	C_6H_6,NH_4^+	*para*-Protonated C_6H_6,NH_4^+	*meta*-Protonated C_6H_6,NH_4^+		$C_6H_5{\cdot}CH_2{\cdot}CH_2NH_3^+$	*para*-Protonated $C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}NH_3^+$	*meta*-Protonated $C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}NH_3^+$
C-1	−0.011	+0.148	−0.008	C-1	+0.060	+0.147	−0.008
	(−0.056)	(+0.350)	(−0.042)		(−0.043)	(+0.359)	(−0.020)
C-2	+0.001	−0.015	+0.148	C-2	−0.003	−0.019	+0.146
	(−0.001)	(−0.060)	(+0.321)		(−0.009)	(−0.018)	(+0.345)
H-2	−0.002	+0.065	+0.079	H-2	−0.002	+0.059	+0.074
C-3	+0.009	+0.154	−0.103 [a]	C-3	+0.010	+0.148	−0.100 [a]
	(+0.015)	(+0.337)			(+0.020)	(+0.326)	
H-3	+0.017	+0.080	+0.100	H-3	+0.018	+0.077	+0.101
C-4	+0.014	−0.105 [a]	+0.150	C-4	+0.012	−0.103 [a]	+0.151
	(+0.029)		(+0.329)		(+0.027)		(+0.331)
H-4	+0.020	+0.104	+0.081	H-4	+0.021	+0.104	+0.079
C-5	+0.009	+0.154	−0.012	C-5	+0.010	+0.148	−0.016
	(+0.015)	(+0.337)	(−0.060)		(+0.020)	(+0.326)	(−0.062)
H-5	+0.017	+0.080	+0.064	H-5	+0.018	+0.077	+0.083
C-6	+0.001	−0.015	+0.149	C-6	−0.003	−0.019	+0.143
	(−0.001)	(−0.060)	(+0.348)		(−0.009)	(−0.018)	(+0.310)
H-6	−0.002	+0.065	+0.092	H-6	−0.002	+0.059	+0.089

[a] sp^3-Hybridized carbon atom.

The calculations for the ions $C_6H_5{\cdot}[CH_2]_n{\cdot}NH_3^+$ ions reproduce the earlier observations that positively charged (and electronegative groups) polarize the π-electron system towards the substituent, with smaller changes at *ortho* and *meta* carbons [5] [see (C)]. There is now considerable evidence for this π-polarization effect, primarily based on ^{13}C chemical shifts for aromatic derivatives.[5,9-11] As pointed out by Craig,[12] approach of an electrophile towards the *para*-carbon atom of $C_6H_5{\cdot}[CH_2]_n{\cdot}NR_3^+$ is disfavoured owing to this π-polarization effect. Thus both the reactant molecule and the Wheland intermediate generally favour *meta*-substitution.



(C)

Although the molecular orbital calculations parallel the product distributions in nitration of $C_6H_5[CH_2]_nN^+(CH_3)_3$, some discrepancies are noted when one compares the energy differences for reaction (i) with partial rate factors (*f*) for nitration and bromination of these derivatives. The partial rate factor measures the rate

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* The calculations for the ammonium in the C_6H_6,NH_4^+ pair indicate that the nitrogen has a charge of −0.4 while each hydrogen atom has a charge of +0.35.

[9] (*a*) D. A. Dawson and W. F. Reynolds, *Canad. J. Chem.*, 1975, **53**, 373; (*b*) W. F. Reynolds and G. K. Hamer, *J. Amer. Chem. Soc.*, 1976, **98**, 7296.

[10] J. Bromilow, R. T. C. Brownlee, R. D. Topsom, and R. W. Taft, *J. Amer. Chem. Soc.*, 1976, **98**, 2020.

[11] W. Adcock, B. D. Gupta, and W. Kitching, *J. Org. Chem.*, 1976, **41**, 1498.

[12] D. M. Bishop and D. P. Craig, *Mol. Phys.*, 1963, **6**, 139.

of reaction at a specific carbon atom, expressed relative to the rate of substitution at a specific carbon atom of benzene, measured under identical conditions.[13] It is related to the substituent effect on the free energy of activation, $\delta\Delta G^\ddagger$, at the given position i by the equation $\delta\Delta G_i^\ddagger = -RT \ln f_i$. These data are summarized in Table 3, along with partial rate factors estimated from the calculations.

TABLE 3

Calculated (from $\delta\Delta G_i = -RT \ln f_i$) partial rate factors for ring protonation of $C_6H_5\cdot[CH_2]_n\cdot NH_3^+$ and experimental partial rate factors for nitration and bromination of $C_6H_5\cdot[CH_2]_n\cdot N(CH_3)_3^+$

System ($R = H$ or CH_3)		$\log f_m$	$\log f_p$
$C_6H_5\cdot NR_3^+$	Calculated	−77.9	−81.0
	Nitration [a]	−7.04	−7.66
	Bromination [b]	−5.23	−5.23
$C_6H_5\cdot CH_2\cdot NR_3^+$	Calculated	−63.0	−64.3
	Nitration [c]	−4.16	−4.80
	Bromination [c]	−2.68	−2.77
$C_6H_5\cdot CH_2\cdot CH_2\cdot NR_3^+$	Calculated	−48.8	−47.0
	Nitration [c]	−1.20	−0.22
	Bromination [c]	−1.06	+0.185

[a] M. Brickmann, J. H. P. Utley, and J. H. Ridd, *J. Chem. Soc.*, 1965, 6851. [b] A. Gastaminza, J. H. Ridd, and F. Roy, *J. Chem. Soc.* (*B*), 1969, 684. [c] R. Danieli, A. Ricci, H. M. Gilow, and J. H. Ridd, *J.C.S. Perkin II*, 1974, 1477.

The calculated and experimental partial rate factors generally show similar trends as n is varied from 0 to 2, particularly with respect to the change from *meta* to *para* preference between $n = 1$ and $n = 2$. However, the calculations grossly overestimate the experimentally observed deactivating effects of positive poles. Although this may be partly due to the fact that the positive charge on the ring is only partially developed in the transition state, it must mainly reflect solvation effects.[4] Solvation has been noted to attenuate effects of ' chemically inert ' substituents in benzene derivatives by factors of 2—10,[14] although the order of substituent effects is maintained.[4] However, the calculations overestimate the effect of positive poles to an even greater extent than for other substituents. A *meta*-nitro-group is calculated to deactivate the Wheland intermediate by 18 kcal mol^{-1} and a *para*-nitro-group deactivates it by 22 kcal mol^{-1},[4] whereas values in excess of 100 kcal mol^{-1} are found for the NH_3^+ group (see Table 1). Thus, the values of $\delta\Delta G^\ddagger$ for electrophilic aromatic substitution at the *meta*- and *para*-positions of nitrobenzene would be expected to be *ca.* five-fold lower than the corresponding values for the anilinium ion. In fact for nitration in concentrated H_2SO_4, $\delta\Delta G^\ddagger(PhNO_2)/\delta\Delta G^\ddagger(PhNMe_3^+)$ has values of 0.92 and 1.02 for *meta*- and *para*-positions, respectively.[15] This must reflect strong solvation and/or ion pairing of the positive pole, drastically reducing its substituent effect in solution.

A second discrepancy concerns the directing properties of NR_3^+ directly attached to the benzene ring. Although both the calculations and the experimental results for nitration indicate a preference for *meta*-attack, the partial rate factors for bromination are identical for *meta*- and *para*-attack. Similarly nitration of $C_6H_5NH_3^+$ in 98% H_2SO_4 shows a slight preference for *para* attack.[6] It has been suggested that the nearly equal preference for *meta*- and *para*-substitution in $C_6H_5NR_3^+$ reflects a balance between field effects (favouring *meta*-attack) and electron-releasing conjugative effects of NR_3^+ (favouring *para*-attack);[1] available evidence indicates that NR_3^+ has a conjugative effect similar to alkyl groups.[16-18] However, the STO/3G calculations appear to underestimate this conjugative effect. The conjugative effect of a substituent in a phenyl derivative can be estimated by $\Sigma q_C{}^\pi$, the total change in carbon π-electron density in the phenyl group.[19] The calculations for the anilinium ion indicate $\Sigma q_C{}^\pi = -0.002$ (Table 2); *cf.* −0.008 for toluene.[20] This underestimation of the conjugative effect presumably accounts for the fact that the calculations predict a significant preference for *meta*-protonation of the anilinium ion.

In this regard, it is interesting that the ^{13}C spectrum for the anilinium ion indicates equal *meta*- and *para*-carbon shifts (2.2 p.p.m. to low field of benzene).[5] The π-polarization effect only becomes apparent when one compares the anilinium ion with the isoelectronic toluene molecule, thus isolating the effect of the positive pole.[5] In fact, there is a very close parallel between the ^{13}C chemical shifts for $C_6H_5\cdot[CH_2]_n\cdot NH_3^+$ and the partial rate factors for *meta* and *para* bromination (see Table 4).

TABLE 4

Comparison of phenyl ^{13}C chemical shifts for *meta*- and *para*-carbon atoms in $C_6H_5\cdot[CH_2]_n\cdot NH_3^+$ with partial rate factors for bromination of $C_6H_5\cdot[CH_2]_n\cdot N(CH_3)_3^+$

System	Chem. shift (p.p.m. to low field of $^{13}C_6H_6$) [a]		$\log f$	
($R = H$ or CH_3)	*meta*	*para*	*meta*	*para*
$C_6H_5\cdot NR_3^+$	+2.19	+2.19	−5.23	−5.23
$C_6H_5\cdot CH_2\cdot NR_3^+$	+1.32	+2.13	−2.68	−2.77
$C_6H_5\cdot CH_2\cdot CH_2NR_3^+$	+1.14	−0.15	−1.06	+0.185

[a] From ref. 5.

This suggests the possibility (at present under investigation) of using ^{13}C chemical shifts to predict product distributions in electrophilic aromatic substitution.

In conclusion, molecular orbital and electrostatic calculations of energy changes upon *meta*- and *para*-protonation of $C_6H_5\cdot[CH_2]_n\cdot NH_3^+$ indicate that the

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[13] C. K. Ingold and F. R. Shaw, *J. Chem. Soc.*, 1927, 2918.

[14] R. W. Taft in ' Proton Transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975, p. 31.

[15] J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, ' Nitration and Aromatic Reactivity,' Cambridge University Press, 1971, ch. 9.

[16] (*a*) P. J. Q. English, A. R. Katritzky, T. T. Tidwell, and R. D. Topsom, *J. Amer. Chem. Soc.*, 1968, **89**, 1767; (*b*) A. R. Katritzky and R. D. Topsom, *Angew. Chem. Internat. Edn.*, 1970, **9**, 87.

[17] I. R. Ager, L. Phillips, T. J. Tewson, and V. Wray, *J.C.S. Perkin II*, 1972, 1979.

[18] W. Adcock, J. Alste, S. Q. A. Rizvi, and M. Aurangzer, *J. Amer. Chem. Soc.*, 1976, **98**, 1701.

[19] R. T. C. Brownlee and R. W. Taft, *J. Amer. Chem. Soc.*, 1970, **92**, 7007.

[20] W. J. Hehre, L. Radom, and J. A. Pople, *J. Amer. Chem. Soc.*, 1972, **94**, 1496.

deactivating and *meta*-directing properties of positively charged substituents are due to the electric field effect of the positive pole. The calculations also provide further evidence for π-polarization by positive poles. Calculated and experimental partial rate factors for electrophilic aromatic substitution show parallel trends, although the calculations overestimate the substituent effects of positive poles and apparently underestimate the conjugative effect of NH_3^+ in the anilinium ion.

DETAILS OF CALCULATIONS

All *ab initio* SCF molecular orbital calculations were carried out with an IBM 370/165 computer by using a version of the Gaussian 70 program.[21] An STO-3G basis set, contracted to a minimal basis,[3] was used throughout. A standard geometry was assumed for the Wheland intermediate[22] and standard bond lengths and bond angles were used in other cases.[23]

The calculations for $C_6H_5{\cdot}NH_3^+$ were carried out for a conformation with one N–H bond in a plane at right angles to the plane of the phenyl group. For the calculations for $C_6H_5{\cdot}CH_2{\cdot}NH_3^+$ we assumed a staggered conformation with the C–N bond in a plane at right angles to the plane of the phenyl group, and for $C_6H_5{\cdot}CH_2{\cdot}CH_2{\cdot}NH_3^+$, the C_α–C_β bond was assumed to be in a plane at right angles to the plane of the phenyl ring and the phenyl and NH_3^+ groups to be in an *anti* conformation.

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[21] W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, Gaussian 70, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Indiana.

[22] W. J. Hehre, R. T. McIver, J. A. Pople, and P. von R. Schleyer, *J. Amer.Chem. Soc.*, 1974, **96**, 7162.

[23] J. A. Pople and D. L. Beveridge, 'Approximate Molecular Orbital Theory,' McGraw-Hill, New York, 1970.