The Meta Effect in Organic Photochemistry: Mechanistic and Exploratory Organic Photochemistry[1,2]

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Abstract: The "meta effect" was defined decades ago as transmission of electron density between meta situated groups on benzenoid compounds in the singlet excited state. This contrasts with the well-accepted ortho–para transmission in the ground state. Our early theoretical efforts made use of the relatively primitive computational methodology available at the time but were supported by our experimental studies. The operation of the "meta effect" has been questioned, and the purpose of the present investigation was to make use of the more sophisticated theoretical methods now available. Thus, ab initio computations of *m*- and *p*-methoxybenzyl cations and radicals were carried out at the CASSCF(8,8)/6-31G* level. Similar computations on acetate anion and acetoxy radicals were obtained in order to provide energies of the methoxybenzyl ion pairs and also the radical pairs. This information bears on the initial competition between S_1 heterolysis and homolysis as well as preferences for meta versus para scission. The evidence provided shows that the energetic preference is for heterolysis to give ion pairs rather than radical pairs, and that the S_1 *m*-methoxybenzyl cation is considerably lower in energy than the S_1 *p*-methoxybenzyl cation, thus confirming the earlier more primitive computations. Further, the 3,5-dimethoxybenzyl cation is even more heavily stabilized.

Introduction

More than three decades ago the suggestion was made that in the first excited singlet of aromatics, electron donation and withdrawal contrasted with the common ortho–para transmission so characteristic of ground state chemistry. This conclusion was based on simple Hückel computations available at the time as well as on experimental photochemical observation in a variety of cases, where the meta and para groups were electron-donating as well as where the substituents were electron-withdrawing.

Recently, one example has been restudied and a somewhat modified sequence of events has been postulated. On this basis the "meta effect" has been discounted. It is the purpose of the present paper to present our more recent results.

Background

It was in 1956 that Havinga[3] described a curious and intriguing phenomenon in a study of the hydrolysis of the isomeric *m*- and *p*-nitrophenyl phosphate esters, **1M** and **1P**, respectively. In the dark in neutral solution these compounds were reasonably stable although, as expected, the para isomer hydrolyzed gradually.

In contrast, the meta isomers, stable in the dark, underwent a facile photochemical hydrolysis while the para isomers showed no greater reactivity than in the dark. Note eqs 1 and 2. The corresponding *m*- and *p*-nitrophenyl sulfate esters showed parallel behavior.

That the meta isomer was more photochemically reactive is, of course, the reverse of normal ground state expectation (i.e. ortho–para electron transmission) and thus quite intriguing.
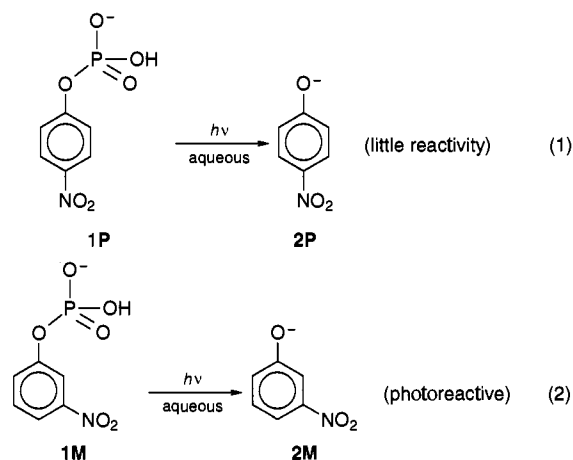
Egbert Havinga noted at the time that the phenomenon was not explicable on the basis of qualitative resonance reasoning.[3]

This prompted us to look at molecular orbital predictions of excited state electron transmission as well as to search for experimental tests. One such example we reported[4] was the photochemical solvolysis of the isomeric *m*- and *p*-cyanophenyl trityl ethers **3M** and **3P**. Note eqs 3 and 4. In this case the meta isomer reacted much more rapidly on irradiation in contrast to its ground state behavior, suggesting preferential meta electron transmission in the singlet excited state. Subsequent to our initial study, many elegant examples of meta transmission of cyano-substituted aromatics have been described by Havinga.[5]

The mirror image situation, having an electron donor substituent present, also was of real interest. Thus we studied the photochemical reactivity of *m*- and *p*-methoxybenzyl acetates

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(1) This is Paper 175 of our photochemical series and Publication 238 of our General Sequence.

(2) For our previous journal article, note: Zimmerman, H. E.; Zhu, Zhaoning, *J. Am. Chem. Soc.* **1994,** *116,* 5245–5262.
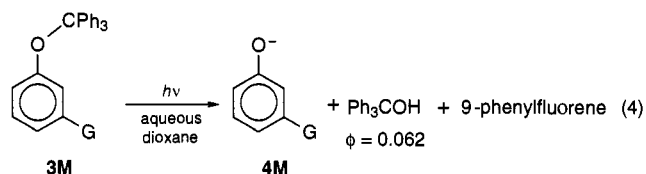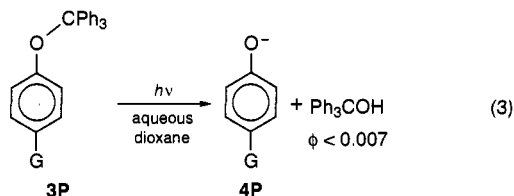
(3) Havinga, E.; De Jong, R. O.; Dorst, W. *Recl. Trav. Chim. Pays-Bas* **1956,** *75,* 378.

(4) Zimmerman, H. E.; Somasekhara, S. *J. Am. Chem. Soc.* **1963,** *85,* 922–927.

(5) (a) Havinga, E.; Kronenberg, M. E. *Pure Appl. Chem.* **1968,** *16,* 137. (b) De-Jone, R. O.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1968,** 1318. (c) Havinga, E.; Cornelisse, J. *Chem. Rev.* **1975,** *75,* 353.

$$\phi < 0.007 \quad (3)$$

$$\phi = 0.062 \quad (4)$$

in aqueous dioxane. It was observed that the *m*-methoxybenzyl acetate (**5M**) led to both heterolysis and homolysis on irradiation while *p*-methoxybenzyl acetate (**5P**) underwent only homolysis. Additionally, it was observed that 3,5-dimethoxybenzyl acetate (**6**) afforded only heterolysis photoproducts.[6] See eqs 5, 6, and 7.

$$(5)$$

$$(6)$$

$$(7)$$
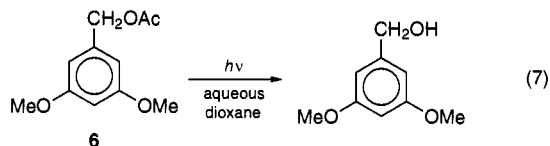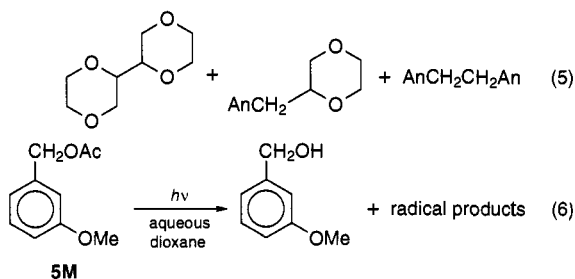
We carried out theoretical studies in parallel to our experimental efforts. At that time, the best computations on molecules of such size were of the Hückel variety. These revealed that in S_1 electron donors transmitted charge to the meta position rather than para while electron withdrawing groups selectively withdrew electron density from the meta site. This, of course, was in accord with the observations of excited state reactivity. At the time, we offered a simple qualitative rationale for this unusual effect in excited state electron transmission which paralleled our computations.

Recently, our early conclusions have been criticized several-fold.[7] First, a redefinition of the "meta effect" has been ascribed to us in which the "meta effect" has been taken as applying only to the reaction of benzylic esters rather than the more general phenomenon of excited state electron transmission. Second, although the preference for meta vs para heterolysis was not challenged, an intermediate step in the heterolysis was proposed in which an initial homolysis of the excited state was followed by electron transfer to give the cation. This reasoning

assumed ground state considerations rather than considering the nature of the initial excited state bond fission.

A main argument used by Pincock[7] as supporting initial homolytic fission of the benzylic esters was that the benzyl pivalates afforded considerably more free radical final products than did the acetates. The idea here is that a pivaloxy free radical once formed will rapidly decarboxylate with formation of the *tert*-butyl radical and thus serve to trap an initial homolysis product.

Clearly, the mechanism needed clarification because of its intrinsic interest. However, additionally it is noted that *m*-methoxy-substituted benzylic carbamate esters have been used as protecting groups, e.g. in the form of $ArCH_2OCONHR$ with NH_2R being the amino acid or peptide being protected.[8]

Results and Discussion

The diversion of the reaction by use of pivalate esters seemed inconclusive. It has been long known that the rate of homolysis in the parallel case of peroxides is enhanced by the presence of potentially stable free radicals such as *tert*-butyl. This rate enhancement results from concerted loss of the CO_2 moiety and formation of the *tert*-butyl radical as homolysis proceeds. Thus pivaloyl peroxides decompose at a greatly enhanced rate relative to acetyl and benzoyl peroxides.[9]

In analogy, the use of the pivalate ester in place of acetate could enhance the rate of homolysis by virtue of concerted fragmentation of the incipient radical pair to give carbon dioxide and *tert*-butyl radical. In peroxide chemistry, fragmentation of the acetoxyl radical is not accelerated since only the methyl radical is formed. Thus in the photochemistry of methoxybenzylic esters substitution of pivalate for acetate should divert the excited state bond breaking from heterolysis in the direction of homolysis.

An approach which seemed likely to elucidate the nature of the mechanism seemed to require an investigation of the energetics of the *m*- and *p*-methoxy-substituted singlet excited states. There has been no question regarding the preferential final formation of the benzylic cations with *m*-methoxy substitution and final free radical formation in the *p*-methoxy case. Rather, the question posed is whether C—O bond stretching and consequent fission in the first excited singlets is heterolytic or homolytic. Our theoretical approach was to evaluate the energetics of the ion pairs and the radical pairs which might be formed.

To obtain reliable results, we employed ab initio computations using GAUSSIAN92.[10] A CASSCF computation with an active space of eight (i.e. four bonding and four antibonding MO's) and a 6-31G* basis set along with geometry optimization was used. It may be said that for molecules of the size of those of interest, this was at the limit of present capabilities. The results are summarized in Table 1.

(6) Zimmerman, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915–9122.

(7) (a) Hilborn, J. W.; Pincock, J. A; Wedge, P. J. *J. Am. Chem. Soc.* **1994**, *116*, 3337–3346. (b) Pincock, J. A.; Wedge, P. J. *J. Org. Chem.* **1994**, *59*, 5587–5595.

(8) (a) Chamberlin, J. W. *J. Org. Chem.* **1966**, *31*, 1658–1660. (b) Birr, C.; Lochinger, W.; Stahnke, G.; Lang, P. *Liebigs Ann. Chem.* **1972**, *763*, 162–172. (c) Barltrop, J. A.; Schofield, P. *J. Chem. Soc.* **1965**, 4758–4765. (d) Birr, C. *Peptides* **1972**, 72–77. (e) Wieland, T.; Birr, C. *Peptides* **1967**, 103–106.

(9) (a) Bartlett, P. D.; Hiatt, R. R. *J. Am. Chem. Soc.* **1958**, *80*, 1399. (b) Prior, W. A.; Smith, K. *J. Am. Chem. Soc.* **1970**, *92*, 5403. (c) Ernst, J. Al; Thankachan, C.; Tidwell, T. T. *J. Org. Chem.* **1974**, *39*, 3614. (d) Prior, W. A.; Davis, W. H.; Stanley, J. P. *J. Am. Chem. Soc.* **1973**, *95*, 4754.

(10) Gaussian 92, Revision A, M. J. Frisch, G. W. Trucks, M. Head-Gordon, P. M. W. Gill, M. W. Wong, J. B. Foresman, B. G. Johnson, H. B. Schlegel, M. A. Robb, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzalez, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart, and J. A. Pople; Gaussian, Inc.: Pittsburgh, PA, 1992.

Table 1. Summary of Calculated Excited Singlet Energies[a,b]

	S₁ *p*-Methoxybenzyl		
ion pair		radical pair	
cation	−382.74564	radical	−382.93565
acetate	−227.24952	acetoxy	−227.18139
ion pair en	−0.12818		
total	−610.1234	total	−610.11704
	S₁ *m*-Methoxybenzyl		
ion pair		radical pair	
cation	−382.76917	radical	−382.93294
acetate	−227.24952	acetoxy	−227.18139
ion pair en	−0.12818		
total	−610.14687	total	−610.11433
	S₁ Dimethoxybenzyl		
ion pair		radical pair	
cation	−496.67850	radical	−496.79878
acetate	−227.24952	acetoxy	−227.18139
ion pair en	−0.12818		
total	−724.05620	total	−724.00483

[a] Both the benzylic cations and radicals are obtained as the first excited states; the acetate and acetoxy species were taken in their ground states. [b] The energy units are hartrees (627.5 kcal/mol per hartree).

The computations aimed at the energies of the radical pairs and the energies for the ion pairs as well. Our approach obtained the CASSCF energies of the *p*-methoxybenzyl radical, the corresponding *m*-methoxybenzyl radical, and also the 3,5-dimethoxybenzyl radical—all in their first excited states. To each energy was added that CASSCF energy of the acetoxy radical in its doublet ground state.

For the ion pairs, the CASSCF energies of the *p*-, *m*-, and 3,5-dimethoxybenzyl cations in their S₁ states were obtained and added in each case to the S₀ CASSCF energy of the acetate anion. However, it is clear that the cation plus anion energies, thus obtained, have assumed that the unlike charges are separated to infinity. A simple illustration results from the CASSCF/6-31G* computation of sodium chloride compared with the sum of CASSCF/6-31G* energies of sodium cation and chloride anion. The optimized sodium chloride ion pair has ca. 127 kcal/mol lower energy (0.203 hartree) than the separated pair with this minimum energy found at 2.4 Å. Due to the size of the methoxy-substituted ion pairs, an alternative approach was devised to obtain the ion-pairing energy. This utilized the sum of the RHF/6-31G* energies of the separate S₀ benzyl cation and acetate anion compared with the similarly calculated energy of the ion pair. To prevent collapse of the ion pair species a fixed geometry was used; this was obtained from AM1 CI(4,4) geometry optimization for S₁. The ion pairing energy was considerably less than that of sodium chloride as might have been anticipated from the more diffuse charges involved.

However, in the use of the benzyl acetate ion pairing energy, there are two sources of error. One is the use of this common species for all the methoxy-substituted ions. The second is the utilization of RHF/6-31G* computations which tend to give higher and less complete energies compared with CASSCF; this approximation was necessitated by the molecular size. Nevertheless, since here we are dealing with the difference in energies of the ion pair relative to the separated ions, the error is minimized. Interestingly, the preferred geometry had the acetate anion in a face-to-face geometry with the two oxygens bissected by the C—CH₂ bond.

In addition, there is an energy of solvation which, in principle, should be included but is more difficult to estimate and is

(11) Berlman, I. B. *Handbook of Fluorescence Spectra of Aromatic Molecules*; Academic Press: New York, 1965.

omitted. However, solvation would tend to lower the energies of the ion pairs relative to the radical pairs in the polar solvents employed. The various components of energies of the radical and ion pairs are given in Table 1. In addition, the total energies are listed.

Three types of comparisons were especially of interest. The first concerns whether the lower energy bond fission on the S₁ hypersurface leads preferentially to the radical pair by homolysis or to the ion pair by heterolysis. Hence, for each of the three systems—*p*-methoxybenzyl, *m*-methoxybenzyl, and 3,5-dimethoxybenzyl—the energy of the radical pair needed to be compared with that of the corresponding ion pair. The second comparison considered the energy of the *m*-methoxybenzyl ion pair versus the *p*-methoxybenzyl ion pair for the monomethoxybenzyl species. The objective here was to determine which S₁ heterolysis process is energetically favored. A third comparison dealt with the comparative energies of the *m*- and *p*-methoxybenzyl radical pairs with the idea being to determine which homolysis would be preferred in S₁.

Turning to the first comparison, namely a determination of the preferred mode of bond fission, we note from Table 1 that the *p*-methoxybenzyl ion pair in the first excited state has a total energy of −610.123 hartrees compared with an energy of −610.117 hartree for the radical pair. The difference of 0.006 hartree, or 3.8 kcal/mol, slightly favors formation of the ion pair. Similar use of Table 1 to compare *m*-methoxybenzyl heterolysis versus homolysis gives −610.147 vs −610.114 hartrees, or a preference for heterolysis of 0.033 hartree or 20.7 kcal/mol. In the case of the 3,5-dimethoxybenzyl ion pair, the difference between the ion pair and radical pair has increased to 0.051 hartree or 32.2 kcal/mol. The energy differences seems likely to be underestimated by a few kcal/mol due to the use of RHF rather than CASSCF energies for the ion pairing energies.

Hence we can conclude that for the *p*-methoxybenzyl system there is little energetic preference for heterolysis compared with the *m*-methoxybenzyl ion pair. However, the 3,5-dimethoxybenzyl ion pair is energetically favored over both of the monomethoxybenzyl systems. The sequence of energies favoring heterolysis is 3.77 kcal/mol (para) < 20.7 kcal/mol (meta) < 32.2 kcal/mol (meta,meta) subject to a constant negative adjustment (vide supra).

The second approach is a comparison of the energetics of the *m*- with the *p*-methoxybenzyl heterolysis. Here Table 1 leads us to a preference of the *m*-methoxybenzyl S₁ cation formation by 0.0253 hartree, or 15.9 kcal/mol. We can conclude that for ion pair formation in the first excited singlet, the meta regioisomer has a distinct advantage.

Finally, we can compare the effect of the methoxy positioning on homolysis. Here the para isomer is preferred, however only by 0.0027 hartree, or 1.68 kcal/mol. This result means that if C—O bond fission is by homolysis, there would be very little difference between the meta and para isomers with the para isomer being the more reactive to the extent that this small energy difference is meaningful.

Thus from our computational results, we are drawn to three conclusions. (1) The first is that excited state heterolysis to afford an ion pair relative to homolysis to give a radical pair becomes increasingly favorable as one proceeds from *p*-methoxy to *m*-methoxy to 3,5-dimethoxy substitution on the benzylic acetate system. (2) The second conclusion is that for heterolysis *m*-methoxy substitution is favored over *p*-methoxy substitution. (3) The third conclusion is that for homolysis, there is a slight energetic advantage to para substitution, and thus to the extent that homolysis were the primary photochemical step, para substitution and not meta substitution would increase reactivity. Hence homolysis as a primary photochemical step is inconsistent

The Meta Effect in Organic Photochemistry

J. Am. Chem. Soc., Vol. 117, No. 35, 1995 8991

Figure 1.

Table 2. Excited State Characteristics of Anisole and Benzyl Acetates

	anisole	p-methoxy-benzyl	m-methoxy-benzyl	3,5-dimethoxy-benzyl
ϕ_f	0.29[c]	0.17[a]	<0.01[a]	<0.01[a]
τ_s, ns	8[c]	6[a]	<1[a]	<1[a]
k_{dtot}, s^{-1}	0.13 × 10⁸	1.67 × 10⁸	>10⁹	>10⁹
ϕ_r		0.016[b]	0.13[b]	0.10[b]
k_r, s^{-1}		2.67 × 10⁶ [d]	>1.3 × 10⁸ [d]	>1.0 × 10⁸ [d]

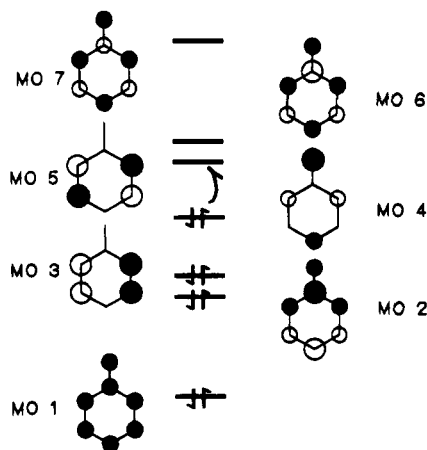[a] From reference 7. [b] From reference 6. [c] From reference 11. [d] This study.

with computation. It is important to note that this reasoning deals with the primary photochemical process and does not preclude modifications of reactivity due to subsequent ground state electron transfer. It is seen that only the first of these three conclusions relies on the assessment of the ion-pairing energy.

It also needs to be noted that the use of acetates rather than pivalates avoids the possibility of concerted fragmentation with loss of carbon dioxide and *tert*-butyl radical. Such a process would complicate the competition between heterolysis and homolysis by enhancing the rate of homolytic fission.

Finally, our use of the ion-pair and radical-pair energies is based on the assumption that these afford the energetic trends on bond-stretching in the first excited states of the benzylic acetates. Therefore, an assessment is made of the relative tendencies of the meta and para excited states to bond stretch heterolytically versus homolytically.

In verbalizing the meta effect, a resort to simple MO considerations is most instructive. Hückel theory is based on molecular topology and is the equivalent of graph theory; in itself, it is exact. Moreover, it is most often closely related to more quantitative computations. In this case our original rationale, based on such simple theory is still valid. Thus in Figure 1 we use the benzyl anion to simulate the excited state electron distribution on a benzene ring substituted with an electron donor. Here we use the $-CH_2$: (i.e. methylene with an electron pair) to typify a donor such as methoxy. We note that the excitation process involves promotion of an electron from MO 4 to MO 5. This is seen to be an excitation of an electron from an MO with no meta electron density to an MO with heavy meta density. Similarly, excitation diminishes the para density markedly and the ortho density is also enhanced. Perhaps the "meta effect" should more properly be termed the "ortho—meta effect". This approximate and semiquantitative picture is supported by more rigorous computation. Thus, a CASSCF-(4,4)/6-31G* calculation on anisole affords a first singlet which has the ortho, meta, and para formal carbon charges as −0.2406 (ortho), −0.2340 (meta), and −0.1379 (para). In addition to confirming the meta electron density transmission from the methoxy oxygen, there is the interesting observation of a similar ortho effect. However, the para electron density is low.

There is some experimental evidence supporting these conclusions. Thus, if one knows the singlet lifetime (τ_s, or $1/k_{dtot}$) and the quantum yield of reaction (ϕ_r) of one of the methoxybenzyl esters, he can solve for the rate of excited state reaction (k_r). Note eq 8. Here k_{dtot} is the total rate of excited

$$k_r = \phi_r/\tau_s = \phi_r k_{dtot} \qquad (8)$$

singlet decay; this includes loss by not only radiationless decay and fluorescence but also reaction. The quantum yield of fluorescence is given by eq 9, where k_f is the "natural" rate of

$$\phi_f = k_f\tau_s = k_f/k_{dtot} \qquad (9)$$

fluorescence as controlled by the molecule's oscillator strength and should not differ much for the various methoxy-substituted compounds, including anisole itself.

Using the data in Table 2 for ϕ_r and τ_s for *p*-methoxybenzyl acetate we can solve eq 8 for the rate of singlet reaction as k_r = 2.67 × 10⁶ s⁻¹. For *m*-methoxybenzyl acetate and 3,5-dimethoxybenzyl acetate with the data available it is only possible to set a lower limit for the excited singlet reaction rates as greater than 1.3 × 10⁸ s⁻¹.

Anisole by comparison has a natural rate of decay (k_f) of 31.9 × 10⁻⁹ s⁻¹, (in methanol) and a fluorescence quantum yield of 0.29 (in hexane). It is clear that anisole and *p*-methoxybenzyl acetate excited singlets have long lifetimes compared with the two meta-substituted compounds. Also, the quantum yields of fluorescence are much greater than the meta compounds which have vanishing fluorescence efficiencies. This is in accord with expectation of the greater rate of reaction of the meta isomers compared with the para and with anisole which does not have a bond fission pathway available. This greater rate of reaction increases k_{dtot} (i.e. decreases τ) and the excited state is depleted before fluorescence can compete effectively. The *p*-methoxy ester reacts only slowly and thus fluorescence competes handily. We remember that the theoretical computations clarify that this experimental rate enhancement is anticipated in an excited state heterolysis but not in a homolysis step.

Hence the theoretical predictions for the excited state primary step and the photophysical data are in accord with the observed photochemistry we reported so long ago with *m*-methoxy substitution enhancing solvolysis.[6]

Conclusion

The theoretical and experimental evidence regarding the character of the first excited singlets of the *m*-methoxy-substituted benzylic acetates clearly indicates that in the primary excited state heterolysis is preferred over homolysis and that increasing meta substitution enhanced heterolysis. Further, if homolysis were the primary step of the excited state and if there was any enhanced reactivity it would have been the para isomer which was more reactive; but this is not the case. Thus, the basic theory of meta electron transmission suggested over three decades ago is supported by the more sophisticated theory possible now.