Spectroscopy and Photochemistry of Phenylacetic Acid Esters and Related Substrates. The Stereoelectronic Dependence of the Aryl/Carboxyl Bichromophore Interaction[1]

Annette M. Kasper, John J. Nash, and Harry Morrison*

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393

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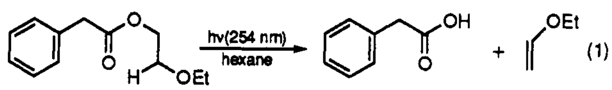
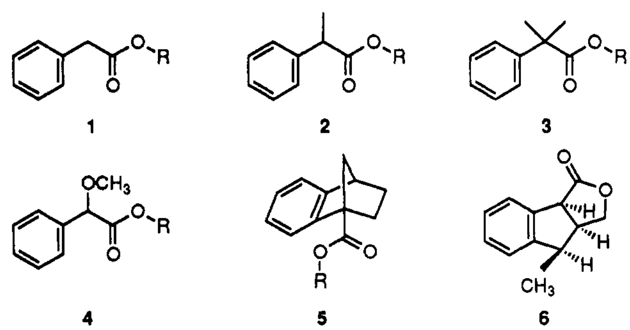
The 254-nm-initiated Norrish Type II photofragmentation of the ethoxyethyl esters of a series of phenylacetic acids (**1b–4b**) has been studied in order to further elaborate the aryl/ester interaction that is photochemically and photophysically evident in these systems. The ethoxyethyl ester of benzonorbornene-1-carboxylic acid (**5**) has also been prepared and studied, as has a rigid tricyclic lactone (**6**) which places the chromophores in an optimal stereoelectronic relationship for interaction. The experimental work is accompanied by Hartree–Fock (HF), Natural Bond Orbital (NBO), and Configuration Interaction with Single Excitations (CIS) calculations on the methyl esters of phenylacetic acid (**1a**) and α-methoxyphenylacetic acid (**4a**). The calculations confirm extensive through-space (TS) and through-bond (TB) interactions between the aryl and ester π^* orbitals but fail to provide conformational or electronic arguments to explain the unusually high reactivity of the α-methoxy series.

As part of our ongoing studies on the photoactivation of distal functionalities in polyfunctional molecules,[1,2] we have been interested in the photoactivation of the ester moiety when it is homoconjugated with a benzene ring.[3] A facile Norrish Type II reaction is generated by 254-nm excitation (eq 1) when appropriate alcohol components



are employed, and the consequent formation of an alkene (together with phenylacetic acid) has been put to good synthetic use.[4] Norrish Type II chemistry involving hydrogen abstraction by the ester from the *O*-methyl group of methyl *O*-methylmandelate has also been observed.[5] Interaction between the ester (or acid) and aryl chromophores is manifested in the UV absorption spectra (relative to toluene) by a large red-shift in the end absorption and a hypochromic perturbation of the aromatic B_{2u} band.[3c,6,7] The fluorescence quantum efficiency decreases, the aryl singlet excited state lifetime is shortened,[3bc,6,7] and (as reported for the carboxylic acid) the phosphorescence quantum efficiency increases.[8] The rate constants for internal conversion and intersystem crossing are enhanced by greater than 2-fold relative to toluene.[3b] A positive correlation of these photophysical effects with the ester photochemistry is evidenced by the diminution in reactivity for those substrates where less perturbation is observed (i.e., phenylpropanoic acid esters and naphthyl acetic acid esters).[3b,c] Triplet quenching and sensitization studies indicate that the Type II reaction derives from the singlet manifold.[3c,5,6]

Scheme 1



a: R = CH_3
b: R = $CH_2CH_2OCH_2CH_3$

The origin of the interaction between the two chromophores, and the stereoelectronic factors which favor this interaction, have been of particular interest to us. Earlier CNDO/S calculations[3b] on phenylacetic acid gave evidence for an n,π^* component of S_1, the existence of which could explain the photochemical reactivity and enhanced k_{ic} and k_{isc} of the corresponding ester. What was particularly fascinating about these calculations was the indication that mixing in S_1 was maximal when the phenylacetic acid was arranged in a conformation with the Ar–CH_2–C=O dihedral angle at 90° and with the CH_2–CO_2H C–C bond parallel to the aryl π system. Reports in the literature supported this indication that the aryl/carboxyl interaction could be affected by conformational factors. Thus, α-substitution by an ethyl group (i.e., 2-phenylbutyric acid) had been shown to enhance the perturbation characteristic of the phenylacetic acid absorption spectrum (attributed to the substituent creating a greater population of conformers in which the aryl and acid orbitals might overlap).[9] Conversely, there was some indication that the bichromophore interaction in indan-

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(9) Tournon, J.; El-Bayoumi, M. A. *J. Chem. Phys.* **1971**, *56*, 5128.

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Scheme 2

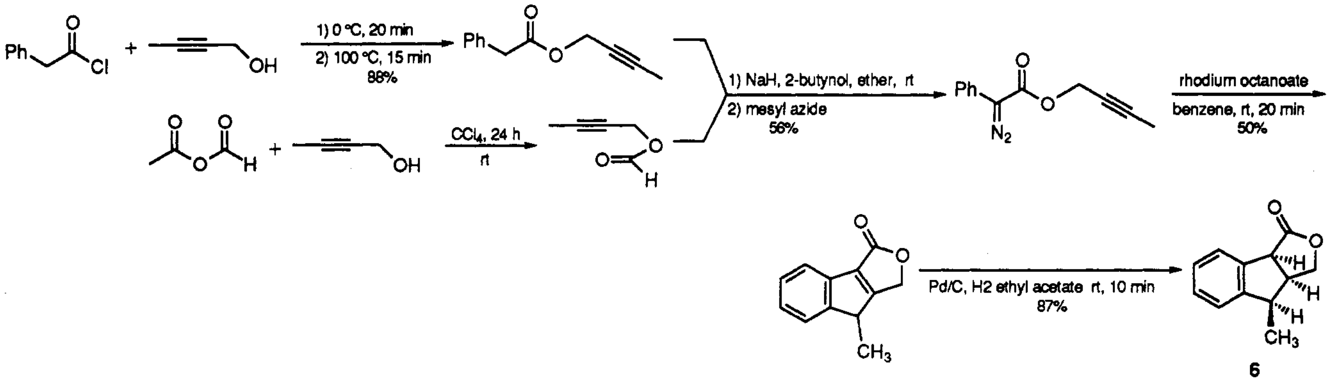

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Table 1. Quantum Efficiencies and Rate Constants for Norrish Type II Fragmentation of the Ethoxyethyl Esters of Compounds 1–5[a]

compound	ϕ_{acid}	k_{acid} (10^6 s^{-1})[b]
1b[3b]	0.040	5.6
2b	0.045	7.7
3b	0.024	7.7
4b	0.047	30.0
5b	0.003	0.23

[a] Photolyses were of 10 mM solutions in cyclohexane using 254-nm excitation. [b] Based upon $^1\tau$ data and the expression $\phi_{acid} = k_{acid}{}^1\tau$.

1-carboxylic acid is reduced relative to the acyclic model.[8] We were particularly struck by the report that α-substitution of methyl phenylacetate by a methoxy group (i.e., methyl *O*-methylmandelate) enhances spectral perturbation and gives rise to an unusually short singlet lifetime (as well as Norrish Type II photochemistry, see above).[5] Conformational factors were one of several possible sources suggested for this effect.

Here, we present the synthesis, spectral properties, and photochemistry of several model compounds (i.e., **1–6**, Scheme 1) designed to test for conformational control of the aryl/carboxyl bichromophore interaction, and the results of additional theoretical studies. We note that the excited state interaction between aryl and amide functions (i.e., as in proteins) has been a subject of recent interest.[10]

Results

Syntheses. The preparation of the phenylacetic acid esters **1–4** and the benzonorbornene-1-carboxylic acid esters **5** were straightforward and followed published procedures. The rigid lactone **6** was prepared as a mixture of 8*R* and 8*S* methyl isomers as outlined in Scheme 2. We assign the major isomer to the structure shown based upon the assumption of hydrogen addition to the least-hindered face.

Photochemistry. The ethoxyethyl esters of acids **1–5** were photolyzed in cyclohexane with 254-nm light and analyzed for the appearance of the corresponding acids by HPLC. Quantum efficiencies are presented in Table 1, together with calculated rate constants for formation of the acids as derived from the singlet lifetimes (see below). Exploratory photolyses of **6** under a variety of conditions (i.e., in hexane, acetonitrile, isopropyl alcohol; with *sec*-butylamine, triethylamine, and *N*,*N*-dimethylethylamine; with dicyanoethylene) gave only traces of dimethylindenes as identifiable products using HPLC and GC analysis.

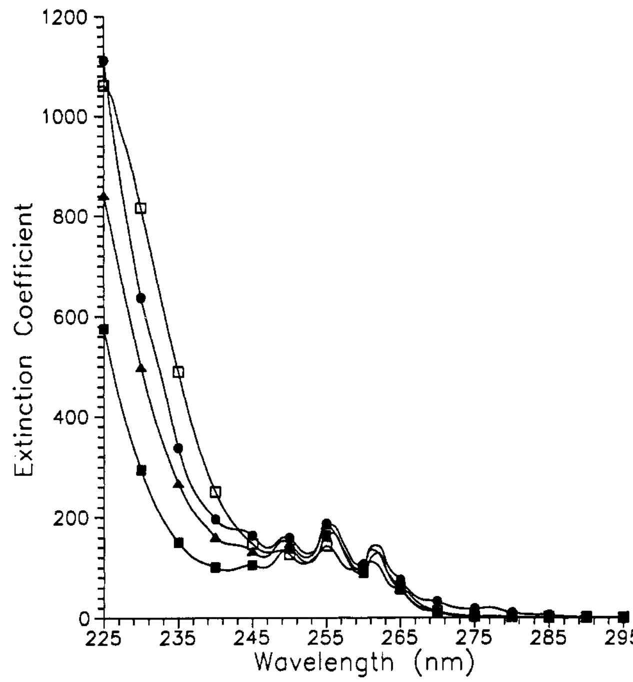

Figure 1. UV Absorption spectra for **1a** (■), **2a** (●), **3a** (▼), and **4a** (□).

Spectroscopy. The ultraviolet absorption spectra of compounds **1a–4a** are presented in Figure 1. All show the characteristic red-shifted end absorption, with the α-substituted derivatives exhibiting markedly larger shifts relative to methyl phenylacetate. This effect is most dramatic for the α-methoxy derivative **4a**. A much more modest effect is seen for methyl benzonorbornene-1-carboxylate, **5a** (relative to benzonorbornene (Figure 2)). Conversely, the tricyclic lactone **6** shows significantly red-shifted end absorption relative to indan, as well as a blue-shifted, hyperchromic B_{2u} transition (Figure 3).

The fluorescence spectra of compounds **1–6** are similar in band position and shape to the spectra of appropriate model compounds, but all except the norbornyl derivative exhibit the expected reduced quantum efficiencies and singlet lifetimes. The data are presented in Table 2. The progressively diminishing fluorescence quantum efficiencies and singlet lifetimes within the series, toluene to *tert*-butylbenzene, has been noted elsewhere.[11]

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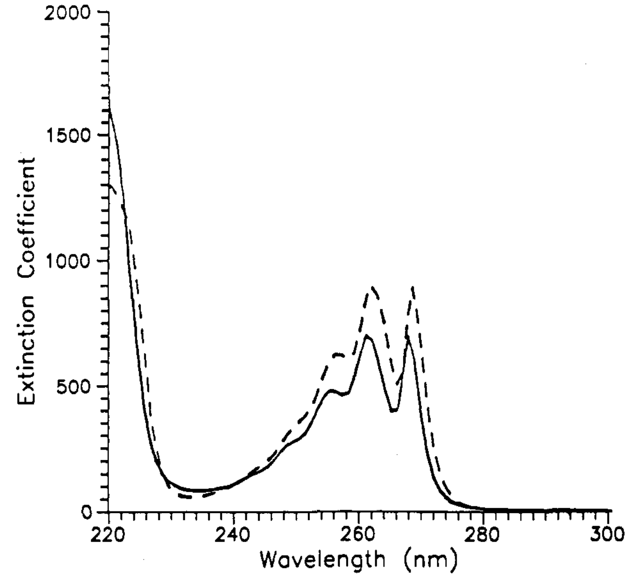

Figure 2. UV Absorption spectra for **5a** (—) and benzonorbornene (- - -).

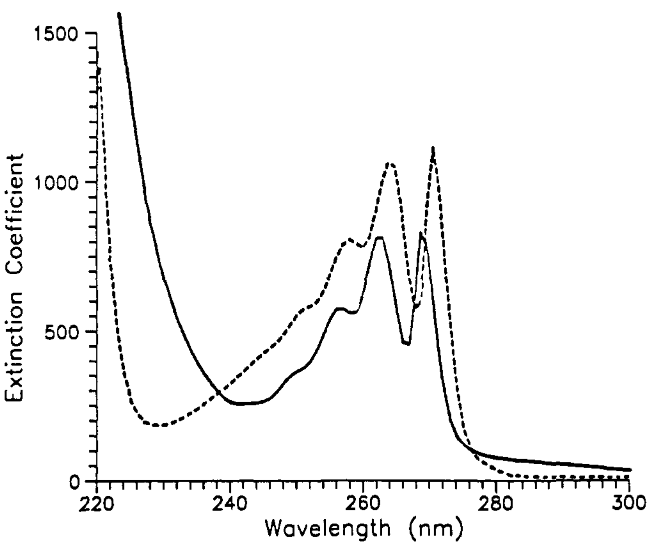

Figure 3. UV Absorption spectra for **6** (—) and indan (- - - -).

Table 2. Quantum Efficiencies of Fluorescence and Singlet Lifetimes for 1-6 and Model Compounds

compound	$\phi_f{}^a$	$^1\tau$ (ns)^b
ethylbenzene	0.085	30
1a	0.019	10.5
isopropylbenzene	0.056	20
2a	0.014	5.8
4a	0.003	1.6
tert-butylbenzene	0.023	11
3a	0.006	3.4
benzonorbornene	0.14	13
5a	0.13	14
indan	0.23	18
6	0.05	5.0

^{a} Hexane solutions; alkylbenzene data from ref 11. ^{b} Cyclohexane solutions for all but indan and **6** which are in hexane; alkylbenzene data from ref 11.

Molecular Orbital Calculations. Geometry optimizations for **1a–5a** and **6** were carried out using the Hartree–Fock (HF) procedure and employing the 3-21G basis set[12]

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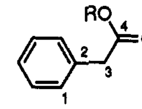

ϕ_1 = 1234

ϕ_2 = 2345

Figure 4. Definition of the dihedral angles, ϕ_1 and ϕ_2, in phenylacetic acid esters.

(i.e., denoted as HF/3-21G). The geometries of **1a** and **4a** (only) were also optimized at the HF/6-31G* level.[13] The optimized dihedral angles, ϕ_1 and ϕ_2 (defined in Figure 4), for the non-rigid model compounds **1a–4a** varied at the HF/3-21G level but were identical for **1a** and **4a** at the HF/6-31G* level (i.e., 104°/97°).

Natural Bond Orbital[14] (NBO) calculations were carried out for **1a** and **4a** in order to determine the individual contributions to the shifts in the aromatic π and π^* orbital energies due to electric field effects, through-space[15] (TS) coupling, and through-bond[16] (TB) coupling.[17] These shifts are shown schematically for **4a** in the correlation diagram presented in Figure 5 (the shifts computed for **1a** are virtually identical to those computed for **4a**). It should be noted that these calculations were performed at the HF/STO-3G[18,19] level using the HF/3-21G optimized values for ϕ_1 and ϕ_2 for **4a** (i.e., 85°/106°) for both molecules (all other geometric parameters were optimized at the HF/3-21G level).

Configuration Interaction with Single Excitations (CIS) single-point calculations were also carried out with the 6-31G* basis set for the lowest-lying (π,π^*) singlet (S_1) and triplet (T_1) excited states for **1a** and **4a** and employing the HF/6-31G* optimized geometries to determine the molecular orbital (MO) contributions within these excited states. There is no significant difference between **1a** and **4a** in either the singlet or triplet excited states. Moreover, the contribution of ester (n,π^*) character in these excited states is minimal.

Discussion

Acyclic Esters. The data in Table 1 indicate that the rate constants for Type II fragmentation of the simple acyclics **1b–3b** are comparable and apparently unaffected by alkyl substitution at the α-carbon. The absorption spectra (Figure 1) for these compounds are quite similar, and their singlet lifetimes are also comparable when adjusted for the "α-substitution" phenomenon[11] (rate

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(14) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

(15) The TS coupling is defined as the coupling due to direct overlap between the localized π (or π^*) orbitals of the aryl and carbonyl groups.

(16) (a) Hoffmann, R.; Imamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 1499. (b) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1. (c) Gleiter, R. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 696. (d) Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245.

(17) For examples of dissection of TS and TB interactions, see: (a) Falcetta, M. F.; Jordan, K. D.; McMurry, J. E.; Paddon-Row, M. N. *J. Am. Chem. Soc.* **1990**, *112*, 579. (b) Paddon-Row, M. N.; Wong, S. S.; Jordan, K. D. *J. Am. Chem. Soc.* **1990**, *112*, 1710. (c) Paddon-Row, M. N.; Wong, S. S.; Jordan, K. D. *J. Chem. Soc. Perkin Trans. 2* **1990**, 417. (d) Paddon-Row, M. N.; Wong, S. S.; Jordan, K. D. *J. Chem. Soc. Perkin Trans. 2* **1990**, 425. (e) Jordan, K. D.; Paddon-Row, M. N. *Chem. Rev.* **1992**, *92*, 395.

(18) Pople, J. A.; Hehre, W. J.; Stewart, R. F. *J. Chem. Phys.* **1969**, *51*, 2657.

(19) We used the STO-3G basis set to avoid the potential problems associated with the virtual orbitals with diffuse basis sets. See, for example: (a) Falcetta, M. F.; Jordan, K. D. *J. Phys. Chem.* **1990**, *94*, 5666. (b) Falcetta, M. F.; Jordan, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 2903.

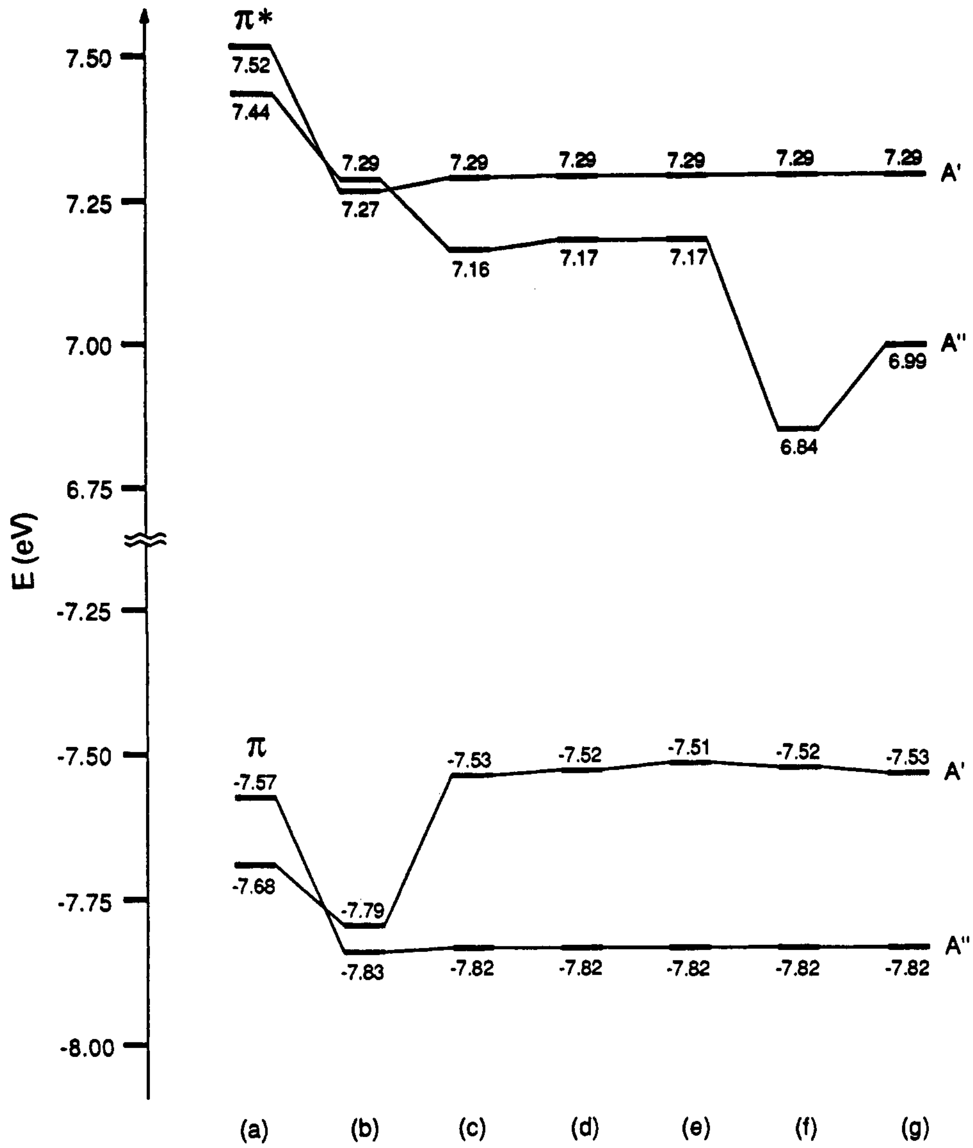

Figure 5. HF/STO-3G NBO interaction diagram for the π and π^* orbitals of **4a**. The steps in the figure are as follows: (a) The noninteracting, localized π and π^* basis NBO's. (b) Inclusion of the electric field caused by the ester group. (c) Inclusion of all hyperconjugative interactions with the C–C linkage. (d) Inclusion of TS interactions with the carbonyl π orbital. (e) Inclusion of TB interactions with the carbonyl π orbital. (f) Inclusion of TS interactions with the carbonyl π^* orbital. (g) Inclusion of TB interactions with the carbonyl π^* orbital.

constants for radiationless decay of **1b**–**3b** are 8.9, 16.0, and 28.0 × 10^7 s^{-1}, respectively). The situation is quite different for α-methoxy substitution (**4b**). The Norrish Type II rate constant is now increased (*ca.* 4-fold) relative to the α-methyl analogue, and though this compound's absorption spectrum is not markedly perturbed, its singlet lifetime of 1.6 ns has been reduced by 72% relative to the same model (the radiationless rate constant also has increased to 59.0 × 10^7 s^{-1}).

Our ab initio calculations do not support a conformational argument to explain these results. At the HF/6-31G* level, the optimized dihedral angles, ϕ_1/ϕ_2, for **1a** and **4a** are identical (104°/97°) and are reasonably close to the "ideal" geometry (i.e., with ϕ_1 and ϕ_2 = 90°) determined from previous CNDO/S calculations for phenylacetic acid.[3b] Even though these calculations are only strictly applicable to gas-phase species, they do suggest that there are no significant conformational (i.e., steric) effects in the *ground* states of these two molecules. This is supported by the fact that, at the HF/3-21G level, the potential energy surface for **1a** with respect to rotation about ϕ_2 is very flat[20] (i.e., at the optimal ϕ_1 of 75°, the barrier for rotation about ϕ_2 is only about 2 kcal/mol).[21] However, it is possible that there are significant conformational changes in the excited states of these molecules. Attempts to carry out geometry optimizations using the CIS method for the singlet excited states of these species were unsuccessful due to the intractable size of the calculations.

As regards electronic effects, the NBO calculations show that at the HF/3-21G optimized geometries, there are significant TS and TB interactions in the aromatic A″ π^* orbitals[22] (LUMO's) of *both* **1a** and **4a**. However, the net shifts due to the sum of both TS and TB interactions are

(20) It should be noted that the potential energy surface is, however, relatively sensitive to rotation about ϕ_1. Our calculations show that, at the HF/3-21G level, a value of about 75° for ϕ_1 is the most energetically favorable.

(21) We have not carried out potential energy surface calculations for **4a**. However, we believe that the potential surface for this molecule is also quite flat with respect to rotation about ϕ_2.

(22) Even though these molecules are asymmetrical, we have used the standard notation for the π and π^* orbitals of the reference compound, toluene.

approximately equal in the two compounds (note that the shifts due to TS coupling are stabilizing whereas those due to TB coupling are destabilizing). Moreover, TS and TB coupling in the occupied π orbitals is negligible in both cases. Thus, the NBO calculations suggest that there are no significant electronic differences between **1a** and **4a** in the ground states of these molecules.

CIS/6-31G* single-point calculations (at the ground state HF/6-31G* optimized geometries) for the (π,π*) singlet and triplet excited states of **1a** and **4a** did not reveal significant ester (n,π*) character in either of these molecules. However, it is possible that the 6-31G* basis set is not sufficiently diffuse to adequately describe the excited states of these species. Although we did not attempt CIS calculations with larger, more flexible basis sets, it does not appear that there are significant electronic differences in the excited states of **1a** and **4a**. We are continuing to explore possible explanations for the unusual rate enhancement by the methoxyl group.

Cyclic Substrates. Our earlier proposal that the coupling of the aryl and ester chromophores has a strong stereoelectronic bias is borne out by the results we have obtained for the rigid benzonorbornyl ester **5b** and the tricyclic lactone **6**. Placement of the ester functionality in the virtually orthogonal relationship inherent in the bridgehead location of **5b** (i.e., ϕ_1/ϕ_2 = 162°/10° at the HF/3-21G level) clearly does reduce the bichromophore interaction. The k_{acid} value drops 20-fold relative to **1b** and the singlet lifetime is essentially identical to that of benzonorbornene. Conversely, **6** (ϕ_1/ϕ_2 = 52°/81° at the HF/3-21G level) shows extensive perturbation of its absorption spectrum (Figure 3) and a reduction in its fluorescence quantum efficiency and singlet lifetime (Table 2), relative to indan. We had hoped that this interaction might be reflected in lactone photochemistry (for example, reduction via electron transfer, or 2 + 2 cycloaddition) analogous to the ester activation already discussed. Those experiments tried to date have so far been unsuccessful.

Summary

The photochemistry of **5b**, and the photophysics of **5b** and **6**, are consistent with our theory-based predictions of the favored geometry for the "superchromophore" formed by homoconjugated aryl esters. α-substitution of alkyl groups in the phenylacetic acid ester series has little effect on the aryl/ester interaction, but an α-methoxyl group has a profound effect. Theory does not support a stereoelectronic explanation for this "methoxy group effect".

Experimental Section

Chemicals. Pyridine (Fisher), indene (Aldrich), and indan (Aldrich) were distilled. Benzene (Fisher) was distilled from sodium. Ether (Mallinckrodt) was distilled from sodium benzophenone ketyl. Spectrograde hexane, cyclohexane, and methanol (Burdick and Jackson, distilled in glass) were used without further purification and were stored under argon. The following chemicals were used as received: Aldrich: 2-butyn-1-ol, 2-ethoxyethanol, 2-indanone, methanesulfonyl chloride, α-methoxyphenylacetic acid, 5% Pd on carbon, 10% Pd on carbon, phenylacetyl chloride, 2-phenylpropanoic acid, sodium formate, sodium hydride; Alfa: n-butyllithium (2.5 M in n-hexane), α,α-dimethylphenylacetic acid; Baker: p-toluenesulfonic acid; EM Science: carbon tetrachloride, iodomethane; Mallinckrodt: acetyl chloride; MCB: phenylacetic acid, sodium azide.

Instrumentation. ^{1}H and ^{13}C NMR spectra were obtained using a General Electric QE-300 (300 MHz) spectrometer. Chemical shifts are reported in ppm relative to TMS. Infrared spectra were obtained using a Perkin-Elmer Model 1800 FT-IR. Ultraviolet spectra were recorded using a Perkin-Elmer Model Lambda 3B spectrophotometer. Fluorescence spectra were obtained on an SLM Aminco Model SPF-500 C spectrofluorimeter. Fluorescence lifetimes were recorded on a Photon Technology International (PTI) Model LS-100 spectrometer. High pressure liquid chromatography (HPLC) was performed using a Varian Model 6000A system with a UV 100 detector (254 nm) interfaced to a Hewlett-Packard Model 3393A digital integrator. HPLC analyses were carried out using an Alltech Econsil C_{18} column (4.6 mm × 25 cm, 10 μm). All HPLC analyses utilized an eluent consisting of 50% methanol, 49% water, and 1% acetic acid at a flow rate of 1–2 mL/min. Low resolution mass spectra were obtained using a Finnigan Automated Gas Chromatograph EI/CI Mass Spectrometer. High resolution spectra were recorded on a Kratos Model MS-50. EI mass spectra were recorded at 70 eV. CI spectra were recorded at 70 eV with isobutane gas at a pressure of 0.30 torr. Gas chromatography utilized a Varian Model 3300 chromatograph for preparative work and either a Varian Model 3700 or a Hewlett-Packard 5710A FID chromatograph with Hewlett-Packard 3390A digital integrators for quantitative studies. Columns used: A (30 m × 0.25 mm, DB-1 capillary (J & W), 0.25 μm film thickness); B (10 ft. × 0.25 in., 10% Carbowax 20M on 60/80 AW-DMCS Chromosorb W). Photochemical studies employed a Rayonet Model RPR-100 reactor and matched quartz photolysis tubes. Deoxygenation was accomplished by bubbling argon through the solutions for at least 15 min. Quantum yield determinations were obtained by using the Norrish type II photochemical conversion of 2-ethoxyethyl phenylacetate to phenylacetic acid.[3b]

Molecular Orbital Calculations. Ab initio calculations were carried out with the Gaussian 90[23] and Gaussian 92[24] programs.

Syntheses. Benzonorbornene,[25] acetic–formic anhydride,[26] and mesyl azide[27] were prepared according to literature procedures.

Methyl Esters. Methyl phenylacetate (**1a**), methyl 2-phenylpropanoate (**2a**), methyl 2-methyl-2-phenylpropanoate (**3a**), methyl α-methoxyphenylacetate (**4a**), and methyl benzonorbornene-1-carboxylate (**5a**) were prepared by refluxing their corresponding acids in methanol and concentrated sulfuric acid. Typical workup involved the addition of water, extraction into ether, drying of the ether, and distillation. The preparation of **5a** was carried out on a 20-mg scale and filtration through a plug of silica gel was used instead of distillation. These esters were shown to be pure using GC analysis on column A. Spectral data for **1a**,[28] **2a**,[29] **3a**,[30] **4a**,[5] and **5a**[31] matched those reported in the literature.

2-Ethoxyethyl Phenylacetate (1b).[3c] This ester was prepared as described previously and isolated, after molecular distillation (bp 100 °C, 0.1 mmHg) as a colorless oil which was shown to be pure by GC analysis on column A at 155 °C. The ^{1}H NMR spectrum matched that reported[3c] previously: ^{13}C (CDCl$_3$, 75

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MHz) δ 171.6, 133.9, 129.2, 128.5, 127.0, 68.2, 66.6, 64.1, 41.1, 15.0; IR (film) 3032, 2976, 2870, 1736, 1498, 1456, 1386, 1254, 1124, 1042, 962 cm^{-1}.

2-Ethoxyethyl 2-Phenylpropanoate (2b). 2-Phenylpropanoic acid (2.5 g, 16.7 mmol), 2-ethoxyethanol (2.7 g, 30 mmol), and benzene (50 mL) were placed in a 100-mL round-bottomed flask. A few crystals of *p*-toluenesulfonic acid were added and the flask was equipped with a Dean–Stark trap. The mixture was stirred at reflux for 12 h. The reaction mixture was placed in a separatory funnel and washed several times with water to remove the excess 2-ethoxyethanol. The benzene layer was then washed with 10% $NaHCO_3$, dried over sodium sulfate, filtered, and concentrated to give a pale yellow oil. The crude oil was purified by molecular distillation (bp 110 °C, 0.1 mmHg) to afford a colorless liquid (2.85 g, 12.8 mmol, 77%). Analysis of the purified ester by GC on column A at 155 °C showed 2-ethoxyethyl 2-phenylpropanoate to be approximately 99% pure: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (m, 5H), 4.20 (m, 2H), 3.75 (q, J = 7 Hz, 1H), 3.55 (m, 2H), 3.44 (q, J = 7 Hz, 2H), 1.50 (d, J = 7 Hz, 3H), 1.14 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.5, 140.4, 128.5, 127.4, 127.0, 68.1, 66.5, 63.9, 45.3, 18.5, 15.0; IR (film) 3030, 2978, 2874, 1734, 1456, 1202, 1168, 1126, 942, 768 cm^{-1}; MS EI *m/e* (%) 177 (0.77), 119 (12), 105 (100), 91 (14), 77 (24), 72 (70), 59 (11), 51 (9); MS CI *m/e* (%) 223 (100); high resolution MS CI (*m/e*) calcd 223.1334, found 223.1332.

2-Ethoxyethyl 2-Methyl-2-phenylpropanoate (3b). 2-Methyl-2-phenylpropanoic acid (1 g, 6 mmol), 2-ethoxyethanol (1.21 g, 13.4 mmol), and benzene (50 mL) were placed in a 100-mL round-bottomed flask. A few crystals of *p*-toluenesulfonic acid were added and the flask was equipped with a Dean–Stark trap. The reaction was stirred at reflux for 12 h. The reaction mixture was placed in a separatory funnel and washed several times with water to remove the excess 2-ethoxyethanol. The benzene layer was washed with 10% $NaHCO_3$, dried over sodium sulfate, filtered, and concentrated to give a colorless liquid. The crude liquid was purified by molecular distillation (bp 115 °C, 0.1 mmHg) to afford a colorless liquid (1.1 g, 4.6 mmol, 75%). Analysis of the purified ester by GC on column A at 155 °C showed 2-ethoxyethyl 2-methyl-2-phenylpropanoate to be approximately 100% pure: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5H), 4.22 (m, 2H), 3.5 (m, 2H), 3.39 (q, J = 7 Hz, 2H), 1.60 (s, 6H), 1.12 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.5, 144.5, 128.2, 126.5, 125.6, 68.0, 66.4, 63.9, 46.5, 26.4, 15.0; IR (film) 2976, 2870, 2362, 1732, 1602, 1498, 1448, 1388, 1254, 1152, 1100, 1032, 860, 764 cm^{-1}; MS EI *m/e* (%) 191 (0.25), 119 (100), 103 (7), 91 (54), 77 (10), 72 (47), 59 (7), 51 (5); MS CI *m/e* (%) 237 (100); high resolution MS CI (*m/e*) calcd 237.1491, found 237.1486.

2-Ethoxyethyl α-Methoxyphenylacetate (4b). α-Methoxyphenylacetic acid (1 g, 6 mmol), 2-ethoxyethanol (1.7 g, 18 mmol), and benzene (50 mL) were placed in a 100-mL round-bottomed flask. A few crystals of *p*-toluenesulfonic acid were added and the flask was equipped with a Dean–Stark trap. The reaction was stirred at reflux for 12 h. The reaction mixture was placed in a separatory funnel and washed several times with water to remove the excess 2-ethoxyethanol. The benzene layer was washed with 10% $NaHCO_3$, dried over sodium sulfate, filtered, and concentrated to give a pale yellow liquid. The crude liquid was purified by molecular distillation (bp 125 °C, 0.1 mmHg) to afford a colorless liquid (1.2 g, 5 mmol, 84%). Analysis of the purified ester by GC on column A at 155 °C showed 2-ethoxyethyl α-methoxyphenylacetate to be 98% pure: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5H), 4.81 (s, 1H), 4.3 (m, 2H), 3.55 (m, 2H), 3.42 (s, 3H), 3.40 (q, J = 7 Hz, 2H), 1.12 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 136.3, 128.8, 128.7, 127.3, 82.5, 68.2, 66.6, 64.4, 57.5, 15.2; IR (film) 2976, 2874, 2828, 1750, 1456, 1258, 1200, 1178, 1118, 1032, 856 cm^{-1}; MS EI *m/e* (%) 207 (0.29), 193 (0.15), 121 (100), 105 (11), 91 (17), 77 (22), 72 (2), 51(4); MS CI *m/e* (%) 239 (100); high resolution MS CI (*m/e*) calcd 239.1283, found 239.1278.

2-Ethoxyethyl Benzonorbornene-1-carboxylate (5b). Benzonorbornene-1-carboxylic acid[31] (0.05 g, 0.26 mmol), 2-ethoxyethanol (0.071 g, 0.8 mmol), and benzene (2 mL) were placed in a 5-mL round-bottomed flask. A few crystals of *p*-toluenesulfonic acid were added and the flask was equipped with a Dean–Stark trap. The mixture was then heated at reflux for 12 h. The reaction mixture was placed in a separatory funnel and washed several times with water to remove the excess 2-ethoxyethanol. The benzene extract was washed with 10% $NaHCO_3$, dried over sodium sulfate, filtered, and concentrated to give a colorless oil. The oil was purified by flash chromatography using 9:1 hexane/ethyl acetate to afford 0.052 g (0.2 mmol) of a colorless liquid. Analysis of the purified ester by GC on column A at 190 °C showed 2-ethoxyethyl benzonorbornene-1-carboxylate to be approximately 100% pure: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (m, 1H), 7.10 (m, 3H), 4.36 (m, 2H), 3.55 (m, 2H), 3.46 (q, J = 7 Hz, 2H), 3.32 (m, 1H), 2.15 (m, 1H), 2.00 (m, 2H), 1.85 (m, 1H), 1.45 (m, 1H), 1.18 (m, 1H), 1.12 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 147.1, 145.0, 126.2, 125.7, 120.6, 120.5, 68.3, 66.6, 63.7, 58.1, 52.0, 43.3, 31.3, 28.3, 15.1; IR (film) 2974, 1734, 1476, 1458, 1386, 1320, 1268, 1234, 1202, 1126, 1090, 1056; MS EI *m/e* (%) 260 (6), 232 (2), 215 (0.68), 188 (15), 160 (8), 142 (100), 128 (25), 115 (60), 89 (4), 72 (7), 59 (6), 51 (2); MS CI *m/e* (%) 261 (100); high resolution MS CI (*m/e*) calcd 260.1412, found 260.1415.

2-Butynyl Phenylacetate.[32] Phenylacetyl chloride (6.9 g, 44.7 mmol) was added dropwise at 0 °C to 3.13 g (44.7 mmol) of 2-butyn-1-ol. The solution was warmed to room temperature and then warmed to 100 °C for 15 min. The dark brown oil was vacuum distilled to afford 17.9 g (bp 116–120 °C, 95%) of a light yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34 (m, 5H), 4.67 (q, *J* = 3 Hz, 2H), 3.68 (s, 2H), 1.8 (t, *J* = 3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 133.5, 129.2, 128.4, 127.0, 83.2, 72.9, 53.9, 40.9, 3.5; IR (film) 2250, 1742 cm^{-1}. The spectral data are consistent with those obtained by Padwa.

2-Butynyl-1-formate.[32] Acetic–formic anhydride (7.04 g, 80 mmol) in 25 mL of carbon tetrachloride was added to a solution of 2-butyn-1-ol (5.6 g, 80 mmol) over 15 min. The reaction was then stirred for 24 h. The solution was transferred to a separatory funnel and washed with saturated $NaHCO_3$, dried over magnesium sulfate, and concentrated. The crude oil was distilled (bp 130–145 °C) to afford a colorless liquid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (s, 1H), 4.75 (s, 2H), 1.80 (s, 3H). The spectral data are consistent with those obtained by Padwa.

2-Butynyl 2-diazophenylacetate.[32] A 25-mL round-bottomed flask, equipped with a nitrogen inlet, was charged with sodium hydride (0.608 g, 60% dispersion in mineral oil), 2-butynyl phenylacetate (0.9 g, 5 mmol), 2-butyn-1-yl formate (1.472 g, 11.8 mmol), and 2-butyn-1-ol (1.53 g, 22 mmol) at 0 °C and the mixture allowed to stir overnight at room temperature. To the reddish-brown mixture was added mesyl azide (1.82 g, 15.2 mmol) in 5 mL of ether. The solution turned a milky-tan color. The reaction was stirred for an additional 2 h and then concentrated. Methylene chloride (100 mL) was added to the residue, and the solution placed in a separatory funnel. The organic layer was washed with 10% NaOH (50 mL), and the aqueous layer was extracted with methylene chloride (2 × 25 mL). The extracts were combined, dried over magnesium sulfate, filtered, and concentrated. The crude orange oil was purified by column chromatography (5% ethyl acetate in hexane) to afford 2-butynyl 2-diazophenylacetate, an orange oil (0.665 g, 3.1 mmol, 62%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.3 (m, 5H), 4.8 (q, *J* = 3 Hz, 2H), 1.9 (t, *J* = 3 Hz, 3H); IR (film) 2924, 2254, 2092, 1702, 1600, 1500, 1438, 1378, 1335, 1246, 1154, 910 cm^{-1}. The spectral data are consistent with those obtained by Padwa.

8-Methyl-3-oxo-3,8-dihydro-1*H*-indeno[1,2-*c*]furan.[32] 2-Butynyl 2-diazophenylacetate (0.1 g, 0.46 mmol) was placed in a 50-mL round-bottomed flask that had been flame-dried and equipped with a nitrogen inlet. Benzene (20 mL) and rhodium(II) octanoate (3 mg) were added to the flask (reaction was complete in a few minutes). The mixture was placed in a separatory funnel, washed with 10% $NaHCO_3$, dried over magnesium sulfate, filtered, and concentrated. The crude product was purified twice by flash chromatography: (1) 15% ethyl acetate in hexane and (2) $CH_2Cl_2/CHCl_3$/ether/hexane (3/1/1/10). Analysis of the purified product by GC on column A at 180 °C showed the product to be approximately 98% pure: ^{1}H NMR ($CDCl_3$,

(31) Wilt, J. W.; Dabek, H. F., Jr.; Berliner, J. P.; Schneider, C. A. *J. Org. Chem.* **1970**, *35*, 2402.

(32) Procedure provided by Professor A. Padwa, personal communication.

300 MHz) δ 7.76 (m, 1H), 7.44 (m, 1H), 7.32 (m, 1H), 5.12 (s, 2H), 3.81 (q, J = 7 Hz, 1H), 1.46 (d, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 176.7, 151.6, 128.7, 128.2, 126.8, 126.7, 126.0, 123.1, 120.3, 68.4, 41.2, 14.9; IR (film) 1760 cm^{-1}. The spectral data are consistent with those obtained by Padwa.

8-Methyl-3-oxo-3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-c]furan (7). 8-Methyl-3-oxo-3,8-dihydro-1*H*-indeno[1,2-*c*]furan (0.01 g, 0.05 mmol) was placed in a 25-mL round-bottomed flask in 10 mL of ethyl acetate. 10% Palladium on carbon (0.01 g) was placed in the flask and the flask evacuated. H_2 gas was introduced into the system, and the reaction monitored by GC using column A at 176 °C. The reaction was complete in about 15 min and the catalyst was filtered and the solvent evaporated. The crude oil was passed through a small plug of silica gel using 10% ethyl acetate in hexane as the eluent to afford 7.9 mg of a 93/7 diastereomeric mixture of the desired product as evidenced by GC analysis. Spectral data were obtained on the mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4–7.0 (m, 4H), 4.40 (m, 1H), 3.95 (m, 2H), 3.48 (m, 2H), 1.35 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.1, 145.9, 136.1, 128.8, 127.8, 124.9, 124.0, 68.5, 49.8, 44.2, 40.2, 13.5; IR (film) 1755 cm^{-1}. This diastereomeric mixture was confirmed by GC/MS using column A. Major isomer: MS EI *m/e* (%) 188 (17), 144 (14), 129 (100), 115 (14); MS CI *m/e* (%) 189 (100). Minor isomer: MS EI *m/e* (%) 188 (15), 144 (12), 129 (100); high resolution MS CI (*m/e*) calcd 189.0916, found 189.0910.

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